NICE National Institute for Health and Care Excellence

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Sent via email

[redacted]
Head of Oncology Business Unit UK
Pfizer Ltd

23 April 2013

Dear [redacted]

Final Appraisal Determination: axitinib for the treatment of advanced renal cell carcinoma after failure of prior systemic treatment

Thank you for lodging Pfizer's 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 lack of transparency in relation to a submission relied upon for the purposes of the guidance is procedurally unfair

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A valid ground one appeal point

1.2. The fact that Pfizer had no adequate opportunity to respond to the additional matters raised by the pharmaceutical industry commentator in response to the ACD, is unfair

I have considered the content of the comments made, as published on the NICE website. It does not seem to me at present that new issues were introduced. The fact that it was challenging to model relative benefits seems to have been properly flagged as an issue in the appraisal before consultation, and of course you had the opportunity to respond and did respond to that consultation not least on this issue.

I understand that fairness can require a further round of comment or consultation after a consultation exercise, where new considerations have been introduced or where a substantially different decision is proposed. You will be aware that the Guide to the STA contains references to this effect. For example, if the ACD had not raised concerns about modelling, a consultee had introduced such concerns, and the committee had based its decision on them, I would have agreed that a complaint of unfairness was valid.

Here, though, a consultee has added material on a pre-existing topic. If the material threw a radically new light on that topic I would still have agreed a complaint was valid. But it is right to be cautious here if appraisals are to terminate in a reasonable period. You yourselves introduced new material on this topic, which you will have hoped would have changed the outcome of the appraisal. It would not have been unfair not to reconsult on that material. Similarly it seems to me that the material introduced by the consultee went to and elaborated on an existing issue, but did not introduce new concerns that you had not had a chance to address.

I would not be minded to refer this point to the appeal panel as valid, but invite your comment before I make a final decision.

1.3. The Scope for this appraisal produces results that inevitably lack certainty.

I cannot see a standalone complaint of procedural unfairness in this point. You will see below that I have agreed that your complaints about a lack of transparency around the ICER judgments are valid, and this complaint seems to me to cover much of the same ground and to be background to those more obviously procedural points.

I am not minded to refer this point to an appeal panel, but I do not mean to suggest that you may not develop the points you have raised here as an aspect of your appeal points 1.4 and 1.7. However I will await your comments before making a final decision.

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1.4. The Appraisal Committee's refusal to find that use of axitinib in post-cytokine patients satisfied the "end of life" criteria on the basis that no comparison with sunitinib or pazopanib had been provided was inconsistent with the Scope for this appraisal

I agree this is a valid ground one appeal point

1.5. The Committee's approach to the assessment of QALY gains occurring in the post- sunitinib group following disease progression and its conclusion that the post-progression model outputs lacked "clinical plausibility" was not transparent

As I understand events, the committee gave certain reasons for doubting that QALY benefits were as substantial as was suggested. You and Professor Hawkins gave reasons why the committee's concerns might be misplaced (although the quotes from Professor Hawkins in your letter seem more to be by way of a statement of disagreement rather than a reason as such). It seems the committee found your material unpersuasive because it repeated its doubts about the QALY benefits in its final analysis.

I note the concern that a failure to provide explanation of these points has prejudiced your ability to understand the conclusions and so is said to be unfair.

I am not presently minded to regard this as a valid appeal point for the following reasons. Most importantly, it seems to me that the committee's procedural obligation is to conduct a fair appraisal process. That does require the main issues in an appraisal to be identified, and an explanation of the Committee's provisional views given, so as to allow for intelligent response. That seems to have happened here, and an intelligent response was made.

Fairness also requires that response is taken into account when preparing the output of the appraisal process, although whether or not it is persuasive is a question of justification (ground 2) rather than fairness.

Past appeal committees have commented on the degree of reasoning required in a FAD, which is not a consultation document. They have commented that a FAD must be sufficiently reasoned to take effect as guidance (in other words, the informed reader must be able to understand what the reasons for the conclusion are, so he or she can take those conclusions into account when exercising clinical judgment). That is a different purpose to being sufficiently reasoned to enable a consultee to understand why consultation comments did not persuade in the final analysis. At present I do not think the obligation of fairness extends that far.

As a second reason, I am unclear what more a committee would reasonably be required to do. The issues were identified and you engaged with them substantively. It seems to me that what remains is a disagreement between experts. To what extent is it possible to give reasons?

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I am not minded to refer this point as valid, but will wait for your comments.

1.6. While the Committee found explanations for post progression QALY gains "clinically implausible", they failed to request attendance by the clinical specialist at the second Appraisal Committee meeting so that any concerns could be discussed

An appeal committee considered a similar point in the appeal in the guidance for Ranibizumab for the treatment of diabetic macular oedema TA 237. While appeal committees do not set precedents I am guided by their past decisions as I expect them to be broadly consistent. I am not minded to refer this point on as valid, in light of the approach taken in TA 237, but invite your comment on that approach before taking a final decision.

1.7. The Appraisal Committee's final conclusions in relation to the cost-effectiveness of axitinib are not stated and its reasons for failing to recommend second-line treatment in patients with advanced or metastatic RCC are therefore unclear, in circumstances where the ICER values appear to fall within the range generally regarded as acceptable in other appraisals.

A valid ground one appeal point

As I agree some of appeal points are valid they will be passed to an appeal panel for consideration. There will be an oral hearing. I would be grateful to receive your comments on the points I am presently not minded to treat as valid within 10 working days of this letter, no later than **Wednesday 8 May,** whereupon I will take a final decision.

Yours sincerely

[redacted]
Appeals Committee Chair
National Institute for Health and Care Excellence