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[redacted]
Health Economics and Strategic Pricing Director
Roche Ltd

25 July 2011

Dear [redacted]

Final Appraisal Determination: Lapatinib or trastuzumab in combination with an aromatase inhibitor for the first line treatment of metastatic hormone receptor positive breast cancer that over-expresses HER2

Thank you for lodging Roche'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 Appraisal Committee's conclusions in relation to (a) the life expectancy of people eligible for trastuzumab in combination with an aromatase inhibitor for first line treatment of metastatic hormone receptor positive breast cancer that over expresses HER2 and (b) the survival gain associated with trastuzumab therapy, are not stated and it is unclear whether the Committee concluded that these criteria for the 'End of Life' advice were met.

I agree that this is a valid appeal point.

1.2 The lack of guidance issued by the Institute in relation to the calculation of small patient populations for the purposes of the End of Life advice is unfair

This point raises issued that were dealt with by the appeal panel in TA227, where the appeal panel found that there was no unfairness caused by the absence of guidance. You were a party to that appeal. I note that the remedy you are seeking is:

Roche requests that NICE issues guidance on the proper approach to calculation of a "small patient population" for the purposes of End of Life advice, consistent with the recommendation of the Appeal Panel in TA227, and that the Appraisal Committee reconsiders this appraisal in the context of that guidance.

The appeal panel in TA227 did not recommend that guidance be issued. It recommended that the Institute review the experience of relevant appraisals, and consider whether further guidance would aid committees. As far as I am aware it has not yet reached a conclusion on this issue. If the criticism is that it should have done so as an aspect of general fairness, that issue would seem to have been decided in TA227. If the criticism is that the Institute should have done as the appeal panel recommended, then assuming for now that that is a point which can be raised in an appeal (and I have my doubts, as it is a criticism that goes to an action of the Institute, not the appraisal committee) as the appeal decision was only published in June 2011 I doubt that the criticism can stand. There is no suggestion that the appeal panel in TA227 thought that appraisals should be put on hold whilst the issue was considered. And finally it seems to me that the appraisal committee cannot be criticised for not having taken into account guidance which has not been (and may never be) issued.

Accordingly at present I am minded to rule this is not a valid appeal point.

Ground 2

2.1 The Appraisal Committee's addition of a further 2,000 patients to the 7,000 population figure estimated by Roche for trastuzumab equates to double counting of patients. These calculations suggest that nearly twice as many mBC patients are potentially eligible for trastuzumab as there are HER2+ mBC patients in the UK. This cannot be reasonably justified in light of the evidence presented and is not a sound a suitable basis for the issuance of guidance to the NHS.

A valid ground two appeal point.

2.2 The Appraisal Committee's statement regarding the overall survival of patients who received aromatase therapy monotherapy in the TAnDEM trial failed to allow for patient cross over

A valid ground two appeal point.

2.3 The Appraisal Committee's statements regarding the overall survival benefit associated with trastuzumab therapy are unreasonable in light of the totality of the data presented

To the extent that you are challenging the conventional reluctance to place reliance on results that are not statistically significant, I doubt that that can be argued not to be capable of reasonable justification. I will allow the point to be considered on the overall arguments made.

2.4 The conclusion by the Appraisal Committee that estimates of progression free survival for the aromatase inhibitor monotherapy in the TAnDEM trial were likely to be too low disregards the fact that the patient population in TAnDEM was different from that in EGF30008

Although I agree this is a valid point, I feel the panel may benefit from further elaboration, if I have understood correctly the argument is that the benefit enjoyed by aromatase inhibitor monotherapy patients is overstated (and hence the incremental benefit enjoyed by trastuzumab combination therapy is understated). The reason the monotherapy patient benefit is overstated is that it is taken from an inappropriate trial. Could you confirm that I have understood correctly, and elaborate further on why the trial was inappropriate, and why the only reasonable approach is to use the TAnDEM data? The panel may also benefit from some discussion of what the consequence of your being correct would be.

Conclusion

As I am minded to agree some of your appeal points are valid I will pass them to an appeal panel for consideration.

If you wish to make any further comment on the point I believe is not valid, together with the clarification requested above, please provide to me within 10 working days from the date of this letter, no later than **Monday 8 August 2011**.

Yours sincerely

[redacted]

Appeals Committee Chair
National Institute for Health and Clinical Excellence