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[redacted]

GlaxoSmithKline Ltd

1 July 2010

Dear [redacted]

Final Appraisal Determination: Lapatinib for the treatment of women with previously treated advanced or metastatic breast cancer

Thank you for lodging GlaxoSmithKline'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 and in accordance with its published procedures as set out in the Institute's Guide to the Technology Appraisal Process.
- Ground 2: The Institute has prepared guidance which is perverse 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

1 The letter from Professor Home dated 16 February 2010 is unclear and does not adequately address the issues raised by the Guidance Executive

I must begin with a general comment, that these appeal points relate to an exchange of correspondence internal to the Institute, taking place after all opportunity for public consultation had passed. It is possible that that exchange could provide evidence for some valid appeal point, in which case I will allow the point to go to appeal, but I am not persuaded that GSK has the standing to complain about the correspondence per se. If, for example, the appraisal committee has not adequately done as the guidance executive asked, that may be a matter for the guidance executive, but it does not seem to me to be a matter for an appellant.

1(a) Misunderstanding of treatment pathway

I am afraid I do not read Professor Home's letter as you do. It seems clear to me that it is trastuzumab that he refers to as being "used out of licensed indication", and not your product. I think you and professor Home would be in agreement that recommending lapatinib in place of trastuzumab would replace a product being used out of licence with one being used in licence, and that that would not be objectionable.

My preliminary view is that this is not a valid ground one appeal point

1(b) No stated basis for concluding that replacing trastuzumab with lapatinib would be difficult to implement.

As I note above, this letter post dates consultation, and as such, even if it is true that it is difficult to respond to that would not seem to be a ground of appeal. I also note that contrary to your letter this concern does seem to be raised in the FAD, in para 4.26.

However, I am minded to allow this point to proceed on the basis that the ACD and associated documents did not give you an opportunity to address this point. (For the avoidance of doubt, I am not

expressing a view on whether that is so, merely that for your complaint to be valid it has to be shifted backward in time and made to apply to the consultation exercise).

My preliminary view is that this is a valid ground one appeal point.

1(c) Committee did not consider women for whom Trastuzumab is unsuitable

I am afraid I do not yet understand the basis for this point. Professor Home's letter is a response to the Guidance executive document and cannot be expected to set out every consideration in the committee's mind. On the face of it the FAD does not appear to have omitted any relevant patient groups. And as a significant part of the difficulty in this appraisal seems to relate to the possibility of substituting Lapatinib for trastuzumab (a substitution which, as I understand it, appears to be at least arguably cost effective, although the committee seem to have identified very significant uncertainty), I am not sure of the relevance of patients who would never have received trastuzumab? Would they not then receive capecitabine, vinorelbine or BCS, and are those options not modelled?

It would help me if you could quote precisely which passages in the letter and FAD are said to give rise to the issue, so that I can make a final determination. Until then my preliminary view is that this is not a valid ground one appeal point.

2 The effect of the direction from the Guidance Executive was that the committee should have considered the cost effectiveness of lapatinib vs trastuzumab in the context of the lapatinib patient access scheme

I am afraid I do not yet understand the basis for this point. Could you highlight for me the passages in the FAD or other documents that are in error, and the analyses in your submissions and/or the ERG report that should have been relied on but were not?

If the committee has not considered an analysis supplied, that could be a valid ground one point, or if it has adopted a different basis for comparison between the different comparators or used the wrong acquisition cost for some of the modelling that could be a valid ground two point, but at present I cannot identify exactly where I can find the error you say has taken place.

3 No explanation is given for the concern that a positive recommendation would potentially displace capecitabine and vinorelbine and this appears to be a matter for implementation not clinical or cost effectiveness

I am afraid I do not accept the premise that implementation is not a relevant consideration when formulating guidance. The committee is under a duty to provide guidance, and that must mean guidance that can be implemented, as otherwise its work is pointless. The committee has identified its

concern, and the reasons for the concern seem obvious, namely that a rule in the form: "If the patient would have received drug A, continue with drug A, if the patient would have received drug B, give drug C," is open to misinterpretation where the criteria for drugs A and B are matters of opinion and the treatment with drug B is hypothetical. And the significance of this is also clear, that the substitution of C for A is not cost effective, and so needs to be prevented.

I would accept that reasonable people might differ on the degree of difficulty here but I cannot see that there is a failure of explanation.

My preliminary view is that this is not a valid ground one appeal point.

4 Even if substitution occurs this should be balanced against cost savings associated with replacement of trastuzumab

I am not sure, in light of the consideration of the blended comparator and the conclusions on the cost effectiveness of substitution of trastuzumab that the committee have not in fact done as you suggest, but I agree it should be considered at an appeal hearing.

In light of the discussion of economic modelling in the FAD, I do not think this can be a ground one point, but it should be considered under ground 2.

5 The conclusion that the trial and clinical populations may differ is not based on reliable evidence.

The observation that a trial population will differ from the population seen in practice is surely a truism. In any case para 4.25 of the FAD merely seems to conclude that there is considerable uncertainty in the data and the conclusions to be drawn from it, and it seems to give a number of specific reasons for that conclusion, all of which appear tenable even if, again, reasonable people might differ on some or all of them. I cannot see that there is any prospect of this being a procedurally unfair conclusion to have drawn, and so my preliminary view is that this is not a valid ground one appeal point.

Conclusion

As I am minded to rule that at least some of your appeal points are valid, I will pass your appeal to the Appeal Panel for consideration.

If you wish to make any further comment on the points that I have indicated that I do not, at this preliminary stage, view as valid, or that I have re-cast, please provide to me this within 10 working days from the date of this letter, no later than **Thursday 15 July**. I will then reach a final decision on the validity of those points.

Yours sincerely

Maggie Helliwell
Appeal Committee Chair
National Institute for Health and Clinical Excellence