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GlaxoSmithKline UK Ltd

1 May 2009

Dear [redacted]

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

Before dealing with your letter I should introduce myself. I have taken over from [redacted] as chair of NICE's appeal panel, as [redacted] has taken up an appointment within the NHS which has required that he stands down from membership of NICE's board. I have read both your initial letter and [redacted] response with care. For ease of reference I will set out my view on all points below, even though some points have already been accepted as valid.

Thank you for having provided more detail as to those parts of your evidence submission and consultation responses that are relevant to each appeal point.

Ground one: Procedural Unfairness

1.1 The Appraisal Committee's refusal to base its recommendations on a comparison with trastuzumab (a standard treatment for advanced or metastatic breast cancer) is contrary to NICE's procedures.

Already accepted as valid.

1.2 The procedure for the appraisal of lapatinib should have been modified to reflect the change in approach resulting from the new supplementary advice from NICE in relation to the appraisal of treatments which may extend the life of patients with a short life expectancy.

Accepted as valid, with thanks for your clarification.

1.3 The Appraisal Committee's application of NICE's Supplementary Advice in relation to the appraisal of treatments which may extend the life of patients with a short life expectancy was overly restrictive and unfair.

In [redacted] original letter he took the view that subpoint 1 of this point raised a procedural issue, but sub-points 2-4 raised issued to do with the treatment of evidence, and were therefore perversity arguments.

On the basis that you wish to argue that the committee's approach was unduly rigid (in other words, that they considered they were bound to follow a policy without consideration of the facts) then I would agree that relates to the process followed, and so should continue as a ground one point. For clarity, arguments that insufficient weight was given to evidence are not ground one points.

1.4 The Appraisal Committee's rejection of the subgroup of patients who had received fewer than three prior treatment regimens lacks transparency.

It is also my view that point (1) of ground 1.4 relates to the weight given to the evidence in this particular appraisal. The relevance of the statistical significance of results can only be that the results should be given more or less weight. I confirm the view that that is a ground two appeal point.

As to the remaining points, I note [redacted] referred to the passage in the Servier judgement which reads "*the reasons are addressed to a technically informed reader; and … the principal purpose and function of a FAD is to give guidance. A FAD needs sufficiently to explain to a technical reader the reasons for the guidance, but it does not need to make a detailed response to every point submitted by consultees"*

It may be that this FAD does not make a detailed response to every point made, but it does not seem to me to be arguable that overall it is so poorly argued that the technical reader would regard it as lacking logic or unintelligible in its reasoning. I therefore also consider that points (2) and (3) should not form part of any appeal.

1.5 The failure to consider fully the additional evidence provided by GSK in response to the publication of the supplementary advice from NICE regarding the appraisal of end of life treatments is unfair.

I note your additional comments as to the form which the suggested further research might take. On further consideration, I agree this is an issue which may be arguable, and which therefore the appeal panel should consider.

1.6 The Appraisal Committee has placed inadequate weight on the medical needs of patients with the disease under consideration

I do not agree that medical need is a factor in a different category from the evidence considered in *Servier* and *Fraser and Short*. It is correct that it is a mandatorily relevant consideration, but the position would still be that, once taken into account, the weight to give to that consideration is a matter for the committee. Reading the guidance as a whole it does not seem to me to be possible to argue that the committee did not consider medical need at all. I would agree medical need is not specifically discussed in the guidance, but for the reasons [redacted] gave I do not think that can form a valid ground of appeal.

1.7 The Appraisal Committee has failed adequately to consider the effect of its recommendations on innovation in the NHS.

I note that many of the factors you mention here are referred to by the committee (possible effect on brain metastases, oral administration, limited treatment options). It seems to me that the were aware of these factors. I note that they do not specifically discuss them in the context of innovation, but it does not seem to me to be arguable that the committee were unaware of the novel features of lapatanib. The weight they chose to give to those features is a matter for them. I do not think this can form a valid ground of appeal.

1.8 The Appraisal Committee has issued recommendations in relation to trastuzumab, which are beyond its remit for this appraisal.

I note your comments on this point. I will ask that the appeal panel or NICE officers will draw them to the attention of the guidance executive as you request.

My decision is that this is not a valid ground of appeal.

Ground 2: Perversity

2.1 The refusal of the Appraisal Committee to make recommendations based on a comparison with trastuzumab has the effect of promoting use of a produce which is unlicensed for this indication and less cost-effective than lapatinib.

Agreed to be a valid point.

2.2 The approach of the Appraisal Committee to the use of lapatinib in patients who have central nervous system metastases is inconsistent with that followed in the Clinical Guideline on breast cancer in relation to trastuzumab and creates a situation that is arbitrary and therefore perverse.

As regards the scope of this initial scrutiny, it is correct that it is not appropriate to resolve issues of fact at this stage. However it is appropriate for me to consider whether an argument is sustainable.

I note your comment concerning consistency. The relationship between an appraisal committee and a GDG was considered in the first appeal against guidance on the primary and secondary prevention of osteoporosis, and so the need for a decision on that issue would not justify allowing this point to proceed. I cannot see how the appeal panel would be able, or could be expected, to adjudicate on whether, in the light of the approach taken by the GDG in respect of trastuzumab, the approach taken in this appraisal is perverse. That would require an investigation of the GDG's work which would be outside the scope of the appeal.

On reconsideration of these points, my decision is that, if you wish, you should be allowed to take the point forward on the simple basis that the decision vis a vis patients with CNS metastases is perverse. I do not think that the comparison with a different treatment and a different body can be relevant, or capable of resolution in this process, and that part of the argument should not be advanced.

I am not sure that the point you made under subpara 2 adds a great deal that is not already within your points 2.1 The comment that trastuzumab should have been a comparator, as its use is recommended in patients with disease progression in the CNS, seems to me to be related to and possibly a subset of the argument allowed in point 2.1, and my decision is that it would be best, and that you should be allowed, to take the point forward under that heading.

2.3 The Appraisal Committee's refusal to consider the use of lapatinib in patients with brain metastates was based on an error and is therefore perverse.

Accepted as a valid ground 2 point.

2.4 The Appraisal Committee's recommendation that trials should be conducted to compare lapatinib in sub groups of patients that included all appropriate treatment comparisons is unethical and therefore perverse.

This is a valid ground 2 point.

Conclusion

This is the final decision on initial scrutiny. The valid appeal points are Ground one: 1.1, 1.2, 1.3, 1.5, ground 2, 1.3, 1.4 (part) 2.1, 2.2 (part) 2.3, and 2.4.

Yours sincerely

[redacted]

Appeals Committee Chair
National Institute for Health and Clinical Excellence