National Institute for Health and Clinical Excellence

Midcity Place
71 High Holborn
London
WC1V 6NA

Tel: 0845 003 7780
Fax: 0845 003 7784

Sent via email

www.nice.org.uk

Dear [redacted]

Final Appraisal Determination: Ranibizumab and Pegaptinib for Age related Macular Degeneration

Thank you for lodging Pfizer's appeal against the above Final Appraisal Determination (FAD). As a preliminary point for information, I have noted your suggestion that the release of the guidance, as it applied to Ranibizumab, should not be delayed. Whilst that was a helpful suggestion in fact there has been an appeal against that guidance, and so both appeals will be heard together.

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 a FAD 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 is referred on to the Appeal Panel.

Ground one

Aspect 1.1

I am not minded to agree this point is arguable. You were aware that an uplift was applied, and that it was 50%. You made the comment that there was no evidence to support that figure and no testing of uncertainty around it. Further, the FAD records that the 50% figure has been derived from an estimate that treatment of the first eye a yields 30% reduction in QALY gain, and a reduction in saving on the costs of blindness. Furthermore the costs of treating the first eye with Pegaptinib are given in the FAD (4.2.4.2). Pages 9 to 17 of the additional analysis commissioned from SHTAC dated 21 September 2007 appears to discuss these figures in detail.

It therefore seems to me that you were aware of the origin and justification of this figure and that there has been no unfairness or failure to follow published procedures. I am not minded to allow this point to proceed.

I would also comment (here and below) that a failure to follow the methods guide is not of itself a ground of appeal. It is failure to follow the guide to the technology appraisal process that is a ground of appeal.

Aspect 1.2

I am not minded to agree this point is arguable. I cannot see procedural unfairness or failure to follow published procedures in the point you have raised. The 30% figure is detailed in the additional analysis which delivers the 50% uplift figure, it appears to me that it has been included in the calculations that produce that figure, and I cannot see that it can be said to be procedurally unfair or that there has been a failure to follow published procedures. I am afraid I do not understand how it is that you are claiming that the 50% figure is not evidence based.

I am not minded to allow this point to proceed.

Aspect 1.3

I agree this point should proceed.

Aspect 1.4

I cannot see unfairness or failure to follow procedures here. You were aware that the committee felt that only 25% of cases would be treated as outpatients. You had and took the opportunity to

challenge that figure. There is no evidence to suppose that your submission was ignored and there is evidence it was taken into account (see page 4 of the document entitled **"**Response to consultee and commentator comments on the second ACD issued December 2007"). I appreciate that you are not satisfied with the results of that taking into account, but that is not a valid ground of appeal.

I am not minded to allow this point to proceed.

Aspect 1.5

I cannot see unfairness or failure to follow procedures here. I am not persuaded that it is automatically procedurally unfair not to perform a sensitivity analysis. Having regard to the large number of sensitivity analyses and alternative scenarios considered in the appraisal and evidenced in the various appraisal documents and reports, I do not think it can be reasonably said that uncertainty has not been addressed. It seems to me that the sensitivity analyses conducted in the evaluation report would form a satisfactory basis for understanding uncertainty in the specific alternative scenarios discussed in the FAD, to the extent that such understanding can be said to bear on unfairness. (See also the reanalysis of your own model which looked at subgroups, and at uncertainty, in some detail.) I do not think it is legitimate to focus on one figure rather than on the overall assessment of uncertainty. I am also unpersuaded that it would be legitimate to focus on costs per QALY for the "early treatment" subgroup, as the committee appears to have decided, in light of its conclusions on the overall cost effectiveness of ranibizumab, that it was not appropriate to make recommendations based on subgroups at all. I am not minded to allow this point to proceed

I note at the end of this point, you suggest that a failure to recommend pegaptanib for patients who are unsuitable for treatment with ranibizumab does not comply with equalities legislation. Please could you provide further information in connection with that argument, noting specifically which protected group it is may be disadvantaged, and how the disadvantage arises, so that I may consider the point.

Aspect 2.1

In effect this ground seeks to characterise the analysis at pp Pages 9 to 17 of the additional analysis commissioned from SHTAC dated 21 September 2007 as perverse. Before I could rule this is a valid ground of challenge, you would need to engage specifically with the reasoning in the additional analysis. My impression at this stage is that your complaint is not logical, since you take the output of the additional analysis (the 50% uplift) and argue that that uplift should be applied only to 30% of the patient population. But, as I understand the analysis, the 50% uplift is in effect an average (ie, it applies to the whole patient population, and the output figure is only 50% because we have considered the whole population.) It could not be valid to apply the uplift averaged across the whole population only to part of that population.

I would assume for present purposes that it could be legitimate, in analytical terms, to have calculated an uplift figure only for the 30% of patients being treated for the first eye, but, unless I have misunderstood, the result would have been very significantly higher than 50%.

I would be grateful for your comments on how the 50% uplift can be applied to only 30% of the population. Presently I am not minded to allow this point to proceed.

Aspect 2.2

I agree this is a valid appeal point.

Preliminary Conclusion

I would be happy to consider any further comments you may wish to make. Any correspondence should be sent to the Institute within two weeks of the date of this letter.

My preliminary view is that aspects 1.3 and 2.2 are arguable appeal points. As I am minded to rule that at least one of your appeal points is valid, an appeal hearing will take place. The Institute will contact you to arrange this in due course.

Yours sincerely

Mark Taylor
Appeals Committee Chair
National Institute for Health and Clinical Excellence