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[redacted]

Pierre Fabre Ltd

30 November 2012

Dear [redacted]

Final Appraisal Determination of vinflunine for the treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract

Thank you for lodging your 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.

Initial View

Ground 1

1.1. In formulating guidance, the Institute has been unfair by not responding to the findings of the previous appeal hearing and has continued to apply inconsistent data quality standards

The previous appeal hearing criticised the committee for considering only patients with a poor prognosis. The appeal panel held that in that case that had amounted to a variation in scope. It advised that the scope included all patients, and that the comparator specified was BSC.

I note that the Committee's new recommendation refers to vinflunine within its marketing authorisation (i.e. for all patients with advanced or metastatic transitional cell carcinoma of the urothelial tract after failure of a prior platinum-containing regimen.) That is a significant change because the committee was expressly directed by the appeal panel to consider all patients (or if it could not to explain why not).

Of the paragraphs in the FAD which you cite as evidence that second line chemotherapy "still take[s] precedence" FAD 4.2 is a recital of what the Committee was told by clinical specialists. FAD 4.3 refers to vinflunine, the only reference to other agents being that there are no proven agents for second line chemotherapy. I cannot read that as a favourable comment on those agents. FAD 4.4 appears to be a conventional and unobjectionable consideration of whether study 302 is generalisable to the patient population. The discussion of this issue seems clear as is the conclusion. I cannot see any inconsistent favouring of other agents, the comments appear to be directed to the important and relevant question of whether the trial population is representative of the whole patient population. FAD 4.5 does not seem to discuss other agents.

Therefore I cannot understand what the alleged inconsistency of treatment is, as I see no "treatment" of other agents at all, nor what relevant issue it is you could not comment on.

I am not minded to refer this point to an appeal panel.

1.2. The Institute has been unfair in the economic evaluation of vinflunine for patients with urothelial cancer that relapse after prior chemotherapy

As I understand this point, you are arguing that if vinflunine were compared with another chemotherapy containing regimen, its incremental cost would be reduced, because both vinflunine and the comparator would incur the non-drug costs of chemotherapy. That must be correct. However the scope for this appraisal clearly states that BSC is to be the comparator, and your previous appeal succeeded on the very point that the committee ought not to make a comparison with second line chemotherapy agents. The appeal panel specifically commented that the new FAD must reflect the fact that the comparator is BSC. Indeed your appeal point 1.1 above seems to take issue with an alleged inclusion of other agents, in a way that I struggle to reconcile with this point.

I am not minded to refer this point to an appeal panel.

Ground 3

3.1 The institute has exceeded its powers by reviewing decisions made by the EMEA and MHRA and drawing different conclusions despite not having the data available or the qualifications to do so.

The Institute and the EMEA have different roles and remits. As I understand it, the EMEA requested the eligible ITT analysis because it had detected that a small number of patients in study 302 were not in fact within the defined patient study population. For its purposes of examining clinical efficacy that was no doubt a reasonable adjustment to make, so that it could be sure the trial data were reliable for its purposes.

The institute generally (and in this case by specific guidance in the previous appeal decision) is interested in the whole NHS patient population. Very commonly this raises the well known issues that trial populations are usually fitter, have fewer co-morbidities, are more motivated, subject to better or at any rate closer medical attention, and so on, and care has to be taken applying trial results, which may well be perfectly adequate for licensing purposes, to the different question of what benefit is likely to be generated in actual clinical practice. Further the Institute is interested in clinical and cost effectiveness, not (as such) clinical efficacy. From its perspective I find it unsurprising that the committee felt that the results from the full study 302 population were more informative for its task than the eligible ITT analysis, and it did not need to identify any flaw in the eligible ITT analysis from the licensing perspective to reach that view. I cannot see that it is arguable that the committee could not decide for itself which analysis was more helpful to it.

Conclusion

As I do not agree your appeal points are valid I am not at this stage passing them to an appeal panel for consideration. However I would be grateful for your response to the points I consider potentially not valid within 10 working days from the date of this letter, no later than **Friday 14 December 2012**, so that I may take a final decision.

Yours sincerely

[redacted]

Appeals Committee Chair
National Institute for Health and Clinical Excellence