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██████████
Managing Director
Pierre Fabre

1 April 2011

Dear ██████████

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

Thank you for lodging Pierre Fabre'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 Pierre Fabre's appeal.

Initial View

Ground one: Procedural Unfairness

1.1 In formulating Guidance the Institute has been unfair by applying inconsistent data quality standards from the manufacturer and commentators on perceived current practice.

You raise a number of points under this heading.

(a) The manufacturer submission was based on a trial reported in a peer reviewed journal and subject to detailed scrutiny by the EMEA and MHRA.

Your point that your data submission was based on a trial published in a peer reviewed journal and also scrutinised by the licensing authorities does not in itself raise any valid ground of appeal. The Institute is carrying out a different assessment to those of the licensing authorities. Publication of a trial in a journal does not in itself establish that the Institute has acted unfairly.

I am therefore minded not to allow this point to proceed.

(b) In the course of the Appraisal vinflunine has been compared with (unlicensed) second line chemotherapy agents in a way that is inconsistent with the Scope for the Appraisal.

A valid ground one appeal point.

(c) The opinions recorded in the FAD about alternative chemotherapy treatments are acknowledged to have various shortcomings.

The fact that the Committee noted that there was a paucity of evidence about use of alternative chemotherapy treatments does not in itself raise a valid ground of appeal (though as outlined above your argument (b) that these treatments were unfairly considered as comparators in the FAD is a valid ground one appeal point).

I am therefore minded not to allow this point to proceed.

(d) No evidence for an alternative existing treatment service was provided to the manufacturer and it is not known if any evidence was provided for the Committee to scrutinise.

A valid ground one appeal point – essentially a subsidiary point your argument (b) above that it was unfair for the Appraisal Committee to compare vinflunine with unlicensed second line chemotherapy.

(e) Comments on the relative toxicity of vinflunine are speculative as the direct clinical experience with vinflunine in bladder cancer available to the Committee was only one patient from an early phase II study in 2001. Objective assessment of relative toxicity was not performed. The toxicity of other classes of agents proposed to the Committee as alternative treatment (platinum or taxanes based) is considerable and both types of drug require extensive pre-medication programmes.

I am not entirely clear what point you are making here. If it is that there is a paucity of evidence on the issue of toxicity that alone cannot form the basis of a valid appeal point – the Committee can only deal with the evidence that it has available. If it is that the Committee's conclusion that other treatments are less toxic than vinflunine is not supported by evidence, the FAD outlines that this evidence came from clinical specialists.

I am therefore minded not to allow this point to proceed.

(To be clear, the argument that no comparison should have been made at all between the toxicity of vinflunine and that of other second line chemotherapy treatments is one that can be made as part of your argument (b) above, which has been allowed to proceed.)

1.2 The Institute has not been consistent or fair in the economic evaluation of new treatment for patients with urothelial cancer that relapse after prior chemotherapy.

Again, you make a number of points under this heading.

(a) The Institute has been inconsistent in recognising in the FAD that there are possible alternative (unlicensed) treatments to vinflunine but relying on economic modelling that compares vinflunine to best supportive care rather than these treatments.

This is a valid ground one appeal point.

(b) The allocation of treatment costs to vinflunine mean that the cost-effectiveness threshold for NICE could only be achieved if the drug cost is reduced to £0. Further research to extend survival with chemotherapy will be futile.

The results of the economic modelling reported in the FAD do not in themselves mean that the Institute has acted unfairly. It does not follow from the outcome of this appraisal that any future treatments will not be cost effective.

I am therefore minded not to allow this point to proceed.

(c) The FAD amounts to a de facto recommendation of the unlicensed second line treatments but these have not been subjected to the same economic comparison with best supportive care as vinflunine.

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 I do not, at this preliminary stage, view as valid, please provide to me this within 10 working days from the date of this letter, **no later than Friday 15 April 2011**. I will then reach a final decision on the validity of those points.

Yours sincerely



Appeals Committee Chair
National Institute for Health and Clinical Excellence