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10 October 2016

Dear

Appeal against Final Appraisal Determination (FAD): Pirfenidone for treating idiopathic pulmonary fibrosis (Review of TA 282).

Thank you for your letter of 30 September 2016 lodging an appeal on behalf of Roche Products Limited against the above FAD.

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:

- 1(a) NICE has failed to act fairly, or
- 1(b) NICE has exceeded powers;
- (2) the recommendation is unreasonable in the light of the evidence submitted to NICE

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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 will 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 (a)

1.1 **In failing to consider the totality of data in respect of 'adults with mild to moderate idiopathic fibrosis' (which is both the full licensed indication and the relevant population as identified in the final scope), and in particular determining that 'the subgroup with a FVC between 80% and 90% predicted was the relevant population for decision making (para 4.5 FAD) the Committee acted contrary to policy and procedures (in particular paragraphs 3.2.2, 5.1.4, 5.10 and 6.2.18 of the Methods guide) with inadequate reasons and unfairly.**

I consider this a valid appeal point.

1.2 The identification of the 80%-90% sub-group at such a late stage of the process, with no consultation or opportunity for relevant evidence or critiquing of evidence to be submitted, was in breach of NICE's obligations of consultation, disclosure and transparency, and contrary to NICE's policy and procedures (in [particular paras 3.3.9 and 3.7.31 of the Guide to the processes of technology appraisal and para 3.1.1 of the Methods Guide)

I am not minded to consider this a valid appeal point. Para 3.7.31 of the Process guide states that when comments and/or new evidence 'leads to a substantial revision of the ACD, involving a major change in the recommendations,

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considerations and/or evidence base [...] will decide whether it is necessary to prepare another ACD'. There was of course no change in the recommendation between the ACD and the FAD. It is correct that the Appraisal Committee used an examination of the 80-90% sub group to reach their final recommendation. However, the ACD noted that the ASCEND trial (referred to in the scope as one of the prime reasons for the review) excluded patients with a predictive FVC greater than 90% and the ERG noted that the ICERs for the group above 80% predicted FVC would have been higher had more people with predicted FVC of over 90% been included (and therefore less favourable to the company's case) (para 4.17). The FAD itself also notes that the company had presented some data with an upper limit of 90% predicted FVC because most of the data was supported by patients with that limit. Given what was said in the ACD and the FAD and the company's own data I struggle to see how it was unfair for the Committee to focus in the FAD on the 80-90% sub group in reaching its conclusion without the need for a further round of consultation on that specific point.

1.3 The Committee's assessment of clinical effectiveness is internally contradictory, inadequately reasoned and unfair and is contrary to its policies and procedures (in particular para 6.1.9 of the Methods guide).

I am not minded to consider this a valid appeal point. Although you point to the statement by the Committee in para 4.10, noting this supplies no reasoning or justification, it seems to me that it is clear from the FAD that para 4.9 and 4.10 should be read together. Para 4.9 provides an explanation as to why the Committee came to the conclusion it did, taking evidence both from the company and the ERG and reaching a (qualified) judgement.

You also refer to the internal inconsistency of the FAD in relation to para 4.10, the summary of the committee's recommendations and para 4.18 which is concerned with cost-effectiveness. However, para 4.10 sets out the Committee's judgement in the light of uncertain evidence (with reasons given in para 4.9), the entry in the summary is beside a heading entitled 'Uncertainties generated by the evidence' where indeed the evidence was not clear to the Committee (although they expressed a qualified judgement) and para 4.18 seems a fair reflection of the points made in para 4.9 -4.10 (for example para 4.10 states 'there was no statistically significant reduction in mortality between pirfenidone compared with placebo).

Ground 2

2.1 Failing to consider the totality of data in respect of adults with mild to moderate idiopathic fibrosis (which is both the full licensed population and the relevant population in the Final Scope) and in particular determining that the

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'sub group of people with an FVC between 80% and 90% predicted was the relevant population for decision making' (para 4.5 of the FAD), was perverse.

I consider this a valid appeal point.

2.2 Identifying the 80%-90% group at such a late stage of the process with no consultation and no opportunity for relevant evidence or critiquing of evidence to be submitted, was perverse. I am not minded to consider this a valid appeal point. The points you raise concern the possible unfairness of the process which are Ground 1 issues and which I have already considered above.

2.3 The Committee's assessment of clinical effectiveness was perverse.

I consider this a valid appeal point.

As I agree at least some of your appeal points are valid they will be passed to an appeal panel for consideration. There will be an oral hearing. The secretariat will be in touch shortly about the arrangements.

I will be happy to consider any further comment you may have on the grounds which I am not minded to regard as valid before making a final decision. Any such comments should be received within 14 days of the date of this letter, by no later than **24 October 2016**.

Yours sincerely

Andy McKeon

Vice Chair
National Institute for Health and Care Excellence