British Thoracic Society

Mr Andy McKeon
Vice chair
National Institute for Health and Care Excellence
10 Spring Gardens
London SW1A 2BU

23 June 2017 - by email

Dear Mr McKeon,

Re: Final Appraisal Determination: Pirfenidone for treating idiopathic pulmonary fibrosis (review of TA282) [ID837]

The British Thoracic Society is grateful to NICE for its detailed work looking at the technology appraisal for pirfenidone for treating idiopathic pulmonary fibrosis. We particularly note the appeal that was sustained by a panel convened on 2 December 2016 and the most recent (June 2017) draft of the relevant Final Appraisal Determination.

The British Thoracic Society would like to appeal against the Final Appraisal Determination for the above mentioned technology appraisal on the following grounds:

Ground 2: The recommendation is unreasonable in the light of the evidence submitted to NICE.

2.1 The Appraisal Committee's refusal to consider the evidence for efficacy of pirfenidone in IPF since the time of the original TA, and the weakness of the health economic argument for choosing an FVC threshold of 80%.

Appropriateness or otherwise of selecting sub groups of patients defined by FVC
We note a great deal of consideration was given to the issue of the appropriateness of subgroup analysis. Point 30, on page 6 of 9 of the appeal panel committee notes states":

> "As far as the reasonableness of considering subgroups is concerned, the Panel tended to agree with Meindert Boysen that in a case where it appeared that use of a product was acceptably cost effective in a whole population, it would not normally be reasonable to look for subgroups within that population where use was cost ineffective. However, it would go too far to make that a general rule."

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We also note however, in point 35:

> "The Appeal Panel did not agree with the Appellant on the effect of the NICE methods guide on the definition of subgroups... In this case, there is nothing suspect about a subgroup using an 80% cut off because the reason for that cut off can be found in current clinical practice, nor was a 90% cut off suspect as that could be seen to derive from the trial data. The Panel concluded that the methods guide does allow NICE to use a treatment threshold to define clinical subgroups."

Cost effectiveness of treating all patients within the licensed indication

When the pirfenidone TA was initially published in 2013 it was based largely on data from the CAPACITY trials. At that stage the US FDA had not licensed pirfenidone and another trial, the ASCEND study, was in progress. Following publication of ASCEND in 2014, pirfenidone was licensed by the FDA and is routinely used at all levels of FVC, including patients with IPF whose FVC is within the 'normal range'. This is also standard practice in many developed countries and this is often commented on by our patients as 'unfair'.

Nonetheless in our system we recognise the need for evidence-based guidance that takes into account health economic analyses as far as they can be made based on the available data. We note however there is a degree of variation in the assumptions made in the analyses. In particular the company estimates a treatment effect of 8 years. The expert panel suggests this effect may only be for 5 years and there is further extrapolation of what the health economic benefit would be if the treatment effect only lasted 2 years. With all of these different variables there appears to be a significant margin of error.

We note that pirfenidone is an expensive drug and there is some doubt from the panel as to the cost effectiveness in the totality of patients with IPF. It has been stated before how, as the first drug shown effectively to impact the natural history of this terminal disease, pirfenidone has given hope to the whole community of IPF patients and their families. Removing access to the drug would lead to significant unrest and likely legal and political challenge. There is a feeling (reflected apart from in other ways by the 2014 FDA decision to license the drug) that the data to support the use of pirfenidone is now far stronger that it was at the time of the 2013 TA.

Cost effectiveness according to FVC cut-off

In point 23 of the December 2016 minutes we read:

> "Professor John Cairns was asked to consider the modelling results that appeared to show that the cost effectiveness for the 50-80% group was essentially the same as for the 50-90% group. He explained that that was a standard result: the larger group masks the cost ineffectiveness of a smaller subgroup. The Committee believed that use would be cost-ineffective in the 80-90% group."

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We do not feel the data justify an attempt to look at the group with an FVC of 80-90% predicted alone. We merely have the comparison of the group having an FVC of 50-80% and the group with an FVC of 50-90% predicted, and it is *accepted* that *cost effectiveness* is *similar* between these two groups.

We note the argument above about exactly where to draw an FVC divide. We strongly feel however that the argument for drawing the threshold at an FVC of 80% based on current practice has a degree of unsatisfactory circularity about it. The threshold of 90% FVC (at which cost effectiveness seems similar to that of 80%) can moreover be justified by the fact that the latest and most robust evidence for the use of use of pirfenidone in IPF comes from the ASCEND study where the top range of FVC was 90%, which as we have stated was published after the 2013 TA and was the trial that convinced the FDA licence pirfenidone in the US, as described above.

Whilst we all realise that expensive drugs such as pirfenidone have to meet health economic thresholds, it is easier to justify to our patients a threshold of 90% above which trial data on efficacy is also less available, especially where there seem to be no significant health economic differences. We feel maintaining the current FVC threshold at 80% may open up justifiable legal challenge by patient groups on the basis of inequality.

Conclusion
We do not feel it is appropriate to maintain the current FVC limit of 50-80% predicted for which we feel there is little justification, as outlined above. We feel the evidence for the efficacy of pirfenidone in IPF is stronger than it was at the time of the original TA and the health economic argument does not appear to exist for choosing an FVC threshold of 80% rather than, say 90%.

We would be grateful for the opportunity to proceed to a written appeal.

Yours sincerely

Honorary Secretary
British Thoracic Society