Sent by email to: xxxx.xxxx@srft.nhs.uk

Xxx xxxx xxxxx

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9 March 2017

Dear xx xxxxxx

**Final Evaluation Determination: Sebelipase alfa for treating lysosomal acid lipase deficiency (LAL D)**

Thank you for your letter of 1 March, lodging your appeal against the above Final Evaluation Determination. I have succeeded xx xxxxxx as vice-chair of NICE. I very well understand your concern as a clinician over the recommendations in the FED but I am required to address the points you raise solely on whether they fall within the grounds for appeal and that you have an arguable case.

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

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.

Initial View

Ground 1 (a)

**1.1(a)**

I assume the point you make in this paragraph is that from your own experience late onset patients who have greatly improved under treatment with sebelipase deteriorate once treatment is withdrawn and this was not taken account of in the Committee’s assessment. I am not minded to consider this a valid appeal point under Ground 1(a). It is clear from the FED that the Committee recognised the benefits of providing treatment to late onset patients and that they considered the proposed managed access scheme which sought to identify the patients who would most benefit and what the starting and stopping criteria would be. In those circumstances it is hard to see how the process was unfair. I have also considered whether this could be an appeal under ground 2 – that the recommendation is unreasonable in the light of the evidence presented. But I am not minded to consider it a valid appeal point under that ground unless you can show that the points you make were submitted in evidence to the Committee and identify in what respect the Committee’s conclusions were unreasonable.

**1.2(a) The reduction in steatosis seen in a greater number if patients on sebelipase alfa compared with placebo (whilst not statistically significant) should be acknowledged [Burton et al 2015].**

I am not minded to consider this a valid appeal point under either Ground 1(a) or Ground 2. Given the reduction in steatosis in the study quoted was not statistically significant when compared with placebo, it is hard to see that the Committee acted unfairly or reached an unreasonable conclusion on how that issue affected the level of uncertainty of the longer term benefits of sebelipase alfa. Moreover it is clear from the FED that the Committee considered that there was a significant reduction in liver fibrosis on the basis of other studies presented by the company (see para 5.6).

**1.3(a) Failure to recommend sebelipase alfa discriminates against patients with LAL deficiency when other equally or less effective enzyme replacement therapies have been funded.**

I am not minded to consider this a valid appeal point. It is in the nature of appraisals that the committee must take a rounded view of costs and benefits and that such judgements will differ depending on the balance between the two. Although NICE should be consistent between appraisals, each appraisal is so dependent on the precise evidence for the costs and benefits of each treatment that it is very difficult to make out an arguable case for inconsistency. For there to be a valid appeal under Ground 1(a) there would need to be an aspect of the process in reaching that decision that was unfair, or a clear and unexplained inconsistency with a truly parallel past appraisal, not simply that the recommendation was disadvantageous to a particular group.

**1.4(a)**

I am not minded to consider that the points you make in this paragraph are valid appeal points under either Ground 1(a) or Ground 2 as negotiation of prices or a review of enzyme replacement therapies lie outside the appeal process which is limited to specific points on the FED.

I should say that NICE values the perspectives of all stakeholders, and in indicating that I am not presently minded to regard your appeal points as valid I am reflecting the necessarily narrow focus of the appeal process. Your engagement with NICE is highly valued.

Please let me have any further observations you may have on the points that I am not minded to consider valid within the next ten working days, **by Thursday 23 March 2017,** and I will then finalise my decision on initial scrutiny.

Yours sincerely

Andy McKeon

Vice-Chair

National Institute for Health and Care Excellence