Sent by email to: xx.xx@uclh.nhs.uk; xx.xxx@gosh.nhs.uk

xx xxx xxx and xx xxx xxx

On behalf of the British Inherited Metabolic Disease Group

9 March 2017

Dear xx xxx and xx xxx

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

Thank you for your letter of 27 February, lodging the BIMDG’s appeal against the above Final Evaluation Determination. I have succeeded xx xxx as vice-chair of NICE.

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)**

It is not entirely clear from your letter on which point under this ground you are appealing. I assume it to be that failure to recommend sebelipase alfa discriminates against patients with LAL deficiency when other equally or less effective enzyme replacement therapies have been funded. However, I am not minded to consider that 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.

Ground 2

**2.1 This decision by NICE has been determined more by the high cost of treatment, rather than insufficient evidence for clinical efficacy in this patient subgroup.**

I am not minded to consider this a valid appeal point. It is clear from the FED that the Committee took into account evidence of clinical efficacy but it is also required to take into account cost and the availability of resources and make a balanced judgement. It would only be a valid point if for example you could present an arguable case that the Committee had, say, underestimated the clinical efficacy (or over-estimated the costs) on the basis of the evidence presented such that the judgement was unreasonable.

**2.2 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].**

It is not entirely clear from your letter which point of the evidence the committee failed to give proper weight to and so reached an unreasonable conclusion but I have assumed it to be the one above. However, I am not minded to consider this a valid appeal point as it stands. 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 reached an unreasonable conclusion on how that issue affected the level of uncertainty of the longer term benefits of sebelipase alfa.

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