Sent by email to: XXXXXXXXXXXXX

XX XXXX XXXX

XXXXXXXXXXXXXXXXXXX

Birmingham Women’s and Children’s NHS Foundation Trust

Birmingham Children’s Hospital

Steelhouse Lane

Birmingham

B4 6NH

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 27 February, lodging your department’s appeal against the above Final Evaluation 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:

* 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.

I can confirm that there will be an oral hearing of the appeal.

Initial View

Ground 1 (a) and (b)

No appeal points.

Ground 2

**2.1 The severity of the infantile presentation and the significance of its alleviation with this therapy has not been fully recognised and therefore the recommendation at least for infantile patients is unreasonable.**

I consider this a valid appeal point on the basis that you consider the Committee has underestimated the clinical benefit of sebelipase alfa, particularly when taken together with your point 2.2.

I should point out however that the reference to section 1.3 of the FED is not in itself evidence that the benefit has been underestimated. This paragraph and phrasing is used routinely in NICE guidance and is intended to avoid cases where commissioners or Trusts withdraw treatment from existing patients on the basis that NICE has not recommended the therapy. It is therefore intended to provide a measure of protection for those patients and to leave decisions about stopping treatment to the patient and their clinician acting jointly and considering only clinical factors.

Similarly, with regard to your reference to para 2.3 of the FED, it seems to me that the Committee did recognise for the purpose of estimating the severity of the disease and the benefits of treatment that virtually all infants presenting with this condition did not live beyond 12 months and that the median age at death was 3 months and that the treatment was potentially life-saving (see paragraphs 5.4 and 5.5).

**2.2 In particular, the degree of systemic inflammation and immune dysfunction which are seen in infant-onset patients has not been considered in the FED.**

I consider this a valid appeal point when taken with point 2.1 above.

**2.3 The ERG’s comment on non-compatibility between LAL-1-NH01 and LAL-CL03 cohorts due to the nature of supportive therapy changing is not valid.**

I am not minded to consider this a valid appeal point. Although the ERG did indeed take that view the Committee also drew on the evidence from experts that any changes in best supportive care had not affected survival and that no child had lived beyond 12 months in the LAL-1-NH01 cohort. (See para 5.5). The Committee also concluded that the ERG view of the difference between treatment with sebelipase alfa and best supportive care was ‘extremely conservative’, and they rejected it (see para 5.17.). As it is the committee's views and guidance which can be appealed rather than the ERG's work, I doubt this can be a valid appeal point.

**2.4 It is unreasonable for the Committee to make a recommendation against funding based on the uncertainty of long-term outcome for the infantile-onset sub group.**

I consider this to be a valid appeal point, on the basis that you consider the Committee’s judgement about the long term benefit of sebelipase alfa to be unreasonable in the light of the evidence.

**2.5 This recommendation goes against previous guidance by NICE where long-term outcome to a treatment was uncertain.**

I am not minded to consider this a valid appeal point. The Committee must assess each technology on its own terms in relation to costs and benefits and the availability of resources. 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. The Committee did consider the positive recommendation they had made for elosulfase alfa when considering their recommendation for sebelipase alfa but it is clear from the FED that there were significant differences in terms of benefit and cost (see para 5.22).

**2.6 This guidance goes against previous guidance given by NICE where a clear subgroup of infantile patients most at risk exists.**

I am not minded to consider this a valid ground two appeal point, because it does not suggest that the conclusion reached on sebelipase alfa is unreasonable in light of the evidence in this appraisal. Unexplained inconsistency between relevantly similar appraisals may be a valid ground one appeal point. However the appeal panel has to understand what it is about the two appraisals that is said to make them so similar that a different outcome suggests that the appraisal process has gone wrong. I noted above that each appraisal depends on the precise evidence for the treatment in question, so that it is difficult to make out an argument that consistency compels the same result in two different appraisals.

If you can expand on what it is that makes the appraisal of asfotase alfa so similar to this appraisal that the results should have been the same, I will consider whether this is a valid ground one appeal point.

**2.7 The significance of treatment effect in older children with LAL deficiency has not been fully appreciated in the guidance.**

I consider this a valid appeal point.

**2.8 It is unreasonable to decline funding for a life-saving treatment based purely on cost when there may be scope for further negotiation with the manufacturer.**

I am not minded to consider this a valid appeal point. Appeals can only be made against a FED on the grounds set out above. The FED is already the culmination of a long process where opportunities were available, and taken by the manufacturer to adjust their price. Whether there is scope for further negotiation does not fall into one of these grounds. However, if the manufacturer were to offer a revised price that seemed likely to result in a change of recommendation before any appeals were completed, the FED would not be issued in its final form and the Committee would be given an opportunity to reconsider their recommendation.

As I agree that at least one of your appeal points is valid it will be passed to an appeal panel for consideration. Please let me have any further observations you may have on those 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