Sent by email to: XXXXXXXXXXXXXXX

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XXXXXX – XXXXXXXXXXXXXXXXXXX

Birmingham Children’s Hospital NHS Foundation Trust

Steelhouse Lane

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31 March 2017

Dear XX XXX

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

Thank you for your letter of 24 March in response to my letter of 9 March to XX XXXX. I note that you are writing on behalf of all four paediatric metabolic centres in England that treat children with LAL-D. I am now able to give you and your colleagues my final view on your appeal points.

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 have not been fully recognised and therefore the recommendation at least for infantile patients is unreasonable.**

I consider this a valid appeal point as set out in my letter of 9 March.

**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 as set out in my letter of 9 March.

**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.**

You made no comments on my preliminary view set out in my letter of 9 March. I confirm that I do not consider this a valid appeal point for the reasons set out in that letter.

**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 a valid appeal point as set out in my letter of 9 March.

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

You made no comments on my preliminary view set out in my letter of 9 March. I confirm that I do not consider this a valid appeal point for the reasons set out in my earlier letter.

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

I have considered this issue further in the light of the points made in your letter of 24 March. However, I am not persuaded that this is a valid appeal point on its own. As I noted in my earlier letter 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. Although the benefits of asfotase alfa and sebelipase alfa may be broadly similar for infants, the Committee must take into account other factors as well as clinical benefit. So it is not therefore possible to argue that because one (albeit very important) aspect is similar to both evaluations that the conclusions should therefore be the same, the fact that I do not consider this a valid appeal point on its own does not prevent you from referring to hypophosphatasia in any explanation of your case under 2.1 above.

**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 as set out in my letter of 9 March.

**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.**

You did not comment on my preliminary view set out in my letter of 9 March. I confirm that this is not a valid appeal point for the reasons set out in that letter.

In summary, my final view is that 2.1, 2.2, 2.4 and 2.7 are valid appeal points. There will be an oral hearing. The Secretariat will already have been in touch about the arrangements for that.

Yours sincerely

Andy McKeon

Vice-Chair

National Institute for Health and Care Excellence