Sent by email to: XXXXXXXXXXXXXXXXXXX

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Alexion Pharma GmbH

Giesshübelstrasse 30

8045 Zürich

9 March 2017

Dear XX XXXXX

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

Thank you for your letter of 1 March, lodging Alexion’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.

Initial View

Ground 1 (a)

**1.1The failure to follow a clearly defined procedure in this HST evaluation is unfair**

I consider this a valid appeal point.

**1.2 There has been no effective consultation on the proposed recommendations for sebelipase alfa in the context of the managed access agreement.**

I am not minded to consider this a valid appeal point. NICE is under two obligations in relation to consultation in the HST: first, it must make sure consultees are sufficiently informed to make an intelligent response, (and it must give them time to do so and consider any response they make). Second, where a draft recommendation changes substantially, it must consider whether to consult again.

In this case the order of events was: (1) publication of an ECD. (2) Submission of a draft MAA. (3) Drafting and publication of a second ECD. (4) Submission of a revised MAA. (5) Publication of the FED. In terms of an ability to make comments on draft proposals that seems in order to me. I do not think that the differences between the second ECD and FED could be such as to call for a third ECD. Your appeal point in essence calls for a right of reply to the committee’s treatment of your MAA, but that is not what NICE’s processes or fairness require.

**1.3 The Committee’s assessment of value for money is unfair and fails to consider the population of patients eligible for treatment within the managed access agreement.**

I consider this a valid appeal point.

**1.4 The Committee has provided no adequate reasons for its conclusions regarding the determination of the population of patients eligible for treatment within the proposed managed access agreement.**

I consider this a valid appeal point.

**1.5 The Committee has failed adequately to take into account the benefits of sebelipase alfa in infants with rapidly progressing LAL D**

I am not minded to consider this a valid appeal point. The points set out in your letter seem to me to have been considered by the committee. A summary of those points, drawn from Alexion’s submission, and the Committee’s consideration is set out at para 5.23

**1.6 The exclusion of a clinical expert from the meeting of the Committee in November 2016 was unfair and is likely to have prejudiced the evaluation.**

I am not minded to consider this a valid appeal point unless you can show that xx xxxxx was the only person with clinical expertise available to the Committee that day and that the Committee were or at least arguably may have been unable to understand the clinical issues without his input. You may wish to consider this past appeal decision where an appeal panel took a restrictive approach to a similar issue:

<https://www.nice.org.uk/guidance/TA360/documents/pancreatic-adenocarcinoma-untreated-metastatic-paclitaxel-albuminbound-nanoparticles-with-gemcitabine-appeal-decision2>

**1.7 The Committee has provided no reason to justify its criticism of the trial data for use of sebelipase alfa in babies presenting before 6 months.**

I am not minded to consider this a valid appeal point. It seems to me that it is clear from the whole paragraph that the Committee did not accept the ERG’s view, particularly with its subsequent comments in 5.17 that the ERG took an extremely conservative view of the benefits of sebelipase alfa compared with best supportive care and its conclusion on that point was not plausible. Moreover, I interpret the lack of robust comparative data as referring to the longer term benefits of whether, for example, the response is maintained and life expectancy fully restored.

**1.8** **The Committee has failed to consider the status of children with juvenile-onset LAL D in accordance with the provisions of the Human Rights Act 1998.**

I consider this a valid appeal point. You will be aware of past appeal panel considerations of similar issues which are published on the NICE website. If you wish to make any legal submissions on this point, I would ask that you put them in writing and send them to the panel not less than 21 days before the appeal hearing. This is to assist the panel to prepare for the hearing.

**1.9 In reaching its conclusions the Committee has failed to take into account relevant evidence**

I consider this a valid appeal point.

Ground 2

**2.1 The Committee’s criticism of Alexion for failing to incorporate collection of non-invasive measures of liver damage in the proposed managed access agreement are unreasonable in circumstances where such measures have not been validated in LAL D**

I consider this a valid appeal point.

**2.2 The Committee’s explanation for preferring the ERG’s utility values does not justify the values selected.**

I consider this a valid appeal point.

As I consider that at least some of your points are valid appeal points I will refer them to an Appeal Panel. I can confirm that there will be an oral hearing. 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, **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