Sent by email to: XXXXXXXXXXXXXXXX

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Alexion Pharma GmbH

Giesshübelstrasse 30

8045 Zürich

31 March 2017

Dear XX XXXXX

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

Thank you for your letter of 23 March in response to mine of 9 March which gave my preliminary views on Alexion’s appeal points against the above Final Evaluation Determination. I can now let you have my final view on those points.

Ground 1 (a)

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

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

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

I have further considered this issue in light of the points made in your letter of 23 March. However, I am not persuaded that this is a valid appeal point given the revised managed access agreement responded to the Committee’s points in their second ECD, which took account of the introduction of a managed access agreement. I do not accept that there is a requirement for a consultation to be "iterative" but even if I am wrong about that the consultation had already been ‘iterative’ with opportunities for consultees to expand their views and answer any questions at Committee meetings. I do not agree that the Moseley case establishes a general rule that rejected proposals must be consulted on. It is explicit that the decision in that case was context dependent and turned on the purpose of the consultation exercise. The Supreme Court perceived that the purpose of that consultation was to allow meaningful public participation in a decision making process with which the public was unfamiliar and that that required information on more than one option to be put forward. Later cases in different contexts have not required consultation on rejected proposals. The NICE process is very different from the Moseley context. Consultation sits as one stage in a process that allows for other forms of stakeholder engagement. While the consultation is open to the public, it does not have the general quasi democratic nature seen in Moseley. The aim is less participation per se, and more informing and improving the decision eventually taken. Therefore I do not agree that fairness requires consultation on proposals that have been rejected.

**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 as noted in my letter of 9 March.

**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 as noted in my letter of 9 March.

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

I have considered this issue further in light of the points you make in your letter of 23 March. I now consider this a valid appeal point.

**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 have further considered this issue in light of the points made in your letter of 23 March. I now consider this a valid appeal point.

**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 have considered this issue further in light of the points made in your letter of 23 March. However, I am not persuaded that this is a valid appeal point. It seems to me clear that the Committee did not accept the ERG’s view of the benefits of sebelipase alfa from the trial data for the reasons set out in my earlier letter. I also consider that the sentence in para 5.4 ‘Furthermore…fully restore life expectancy’ must be read in full and in the context of the whole paragraph which makes clear that the Committee’s concerns were about variability in babies’ responses (two thirds taking part in the trial lived beyond 12 months) and the long term benefits of treatment.

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

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

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

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 as set out in my letter of 9 March.

**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 set out in my letter of 9 March.

In summary therefore my final view is that the following are valid appeal points: 1.1, 1.3, 1.4, 1.5, 1.6, 1.8, 1.9, 2.1 and 2.2. There will be an oral hearing of these points. The Secretariat will already have been in touch about the arrangements for it.

Yours sincerely

Andy McKeon

Vice-Chair

National Institute for Health and Care Excellence