2nd Floor 2 Redman Place

London E20 1JQ

United Kingdom

+44 (0)300 323 0140

Sent by e-mail only: XXXXXXXXXXXXX

FAO XXXXXXXXXXXXX Niemann-Pick UK

Suite 2, Vermont House Concord,

Washington NE37 2SQ

Tuesday 26 March 2024

Dear XXXXXXXXXXXXXX

# Re: Final Draft Guidance – Olipudase alfa for treating acid sphingomyelinase deficiency (Niemann-Pick disease) type AB and type B [ID3913]

Thank you for your letter of 19 March 2024, lodging an appeal against the above Final Draft Guidance (FDG). Dr Chakravarty is temporarily unavailable and so in accordance with paragraph 3.1 of NICE's Guide to the technology appraisal and highly specialised technologies appeal process, I am conducting initial scrutiny on this occasion.

Introduction

The Institute's appeal procedures provide for an initial scrutiny of points that an appellant wishes to raise, to provide an initial view on whether they are within the permitted grounds of appeal ("valid") and are at least arguable. 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, are arguable, and fall within any one of the grounds will your appeal be referred to the Appeal Panel.

You have the opportunity to comment on this letter in order to elaborate on or clarify any of the points raised before I will make my final decision as to whether each appeal point should be referred on to the Appeal Panel.

Initial View

I assess each of your points in turn.

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***Ground 1(a): In making the assessment that preceded the recommendation, NICE has failed to act fairly***

# Appeal point 1(a).1: The Committee’s decision does not fully recognise the significant clinical and life changing benefits of treatment with olipudase alfa

Following careful consideration, I am not minded to refer this appeal point to the Appeal Panel. I understand your argument to be that the Committee has underestimated the clinical benefits of treatment and the evidence that it can overcome disease severity and reverse disease impact. In support of this, you refer to paragraph 3.26 of the FDG, in which the Committee acknowledges, as part of its consideration of whether olipudase alfa is an innovative treatment, that the QALY calculations probably did not fully capture symptoms, and so the benefit of olipudase alfa may be underestimated. It is clear, however, that the committee took this issue into account in its decision-making, concluding that olipudase alfa is innovative in treating ASMD. I cannot see a basis on which the Committee's consideration of this issue was arguably unfair.

You have also argued that the Committee should have taken account of "*the ten-plus years of real-world evidence, which strongly demonstrates a lack of functional decline in patients with longer term use of olipudase alfa*". Again, I cannot see any arguable unfairness in the Committee's approach. The Committee concluded that olipudase alfa improves clinical outcomes associated with ASMD and that treatment effect can continue into the longer term, but becomes more gradual as the person’s condition moves nearer to full-health. The committee did take evidence of longer term effectiveness into account in its decision making, driving its conclusion that a 27.6 QALY gain was considered most plausible.

# Appeal point 1(a).2: The Committee did not consider or fully take into account all available evidence relating to patient and carer QoL and disutilities.

I am minded to refer this appeal point to the Appeal Panel, on the basis that it is arguable that the Committee has acted unfairly if it:

* misrepresented the patient expert's position by stating in paragraph 3.17 of the FDG that "[T]*he patient expert agreed that the driver of carer requirements (and carer disutility) was the health state of the person with ASMD*" and/or
* "*cut short*" patient experts with the consequence that the Committee did not receive sufficient patient testimony to enable the Committee to understand their position.

There are a number of other points made under this appeal point in your letter, which do not seem to me to demonstrate arguable unfairness:

* You refer to a recently published (2024) study by Raebel and colleagues. If this study was not available to the Committee, it was not unfair for the Committee not to have had regard to it.
* You note the Committee's conclusion that an average of 1 carer was appropriate for decision making, and ask that the Committee reconsider the reported patient expert view that an average of 1.5 carers would be more reasonable. It is clear from paragraph 3.19 of the FDG that the Committee did consider that view, but reached a different conclusion. The Committee did not fail to consider it, and so its approach was not arguably unfair. If you consider that the Committee's conclusion on this point was unreasonable, you may re-state this appeal point as a ground 2 point, with an explanation of why you consider the conclusion to be unreasonable (with reference to the rationale for the Committee's conclusion provided in paragraph 3.19 of the FDG).
* You note that the Committee considered the impact of a patient's death on carers qualitatively but not quantitatively and question whether the Committee sufficiently understood the impact. Again, the FDG is clear that the Committee did consider the patient expert evidence on this point and reached a view having considered that evidence. The Committee's approach was therefore not arguably unfair. If you consider that the Committee's conclusion on this point was unreasonable, you may re-state this appeal point as a ground 2 point, with an explanation of why you consider the conclusion to be unreasonable (with reference to the rationale for the Committee's conclusion provided in paragraph 3.20 of the FDG).
* You refer to a study by Song and colleagues. I note that the EAG provided the Committee with specific consideration of this study (see page 431 of the Committee Papers dated 23 October 2023, at page 80 of the EAG's report beginning at page 352 of those papers). Again, therefore, I cannot see an arguable case that the Committee acted unfairly by failing to consider that study.

***Ground 2: the recommendation is unreasonable in the light of the evidence submitted to NICE***

# Appeal point 2.1: The Committee did not give due consideration to the proposed MAA (3.24) and the potential to address uncertainties in clinical benefit, patient, and care disutilities.

I am not minded to refer this appeal point to the Appeal Panel. The Committee can consider a recommendation with managed access only when all three of the following criteria are satisfied:

* the medicine has the plausible potential to be cost effective at the currently agreed price, but the evidence is currently too uncertain, and
* new evidence that could sufficiently support the case for recommendation is expected from ongoing or planned clinical trials, or could be collected from patients having the medicine in clinical practice, and
* these data could feasibly be collected within a reasonable timeframe (up to a maximum of 5 years) without undue burden.

(The Manual, paragraph 6.4.6)

One of the mandatory criteria is therefore that the technology must be plausibly cost effective *at the currently agreed price*, if evidential uncertainties can be resolved. In this case, the Committee explained in paragraph 3.24 that "*at the price the company had chosen to charge, olipudase alfa was not plausibly cost effective*". It was therefore not open to the Committee to make a positive recommendation with managed access. I appreciate that the pricing data is confidential to the Company and therefore may not be available to NPUK; however, without some basis for considering that the proposed data collection would resolve evidential uncertainties with the effect that the technology would become cost effective at its current price, the criteria for a positive recommendation with managed access cannot be met.

Conclusion

The above sets out my initial views on all of your appeal points.

In respect of your points which I am not minded to refer on you are entitled to submit further clarification and/or evidence to me within the next 10 working days, and I will then give a final decision on the points to put before an appeal panel. For the point I am already content to refer on, an oral appeal will be held which is likely to be held remotely.

Once I have made my final decision, and where there is more than one appellant, each appellant will receive the valid appeal points of the other appellants and their redacted appeal letter. This is to enable appellants to avoid duplication at the hearing where there are overlapping appeal points. If the appeal letter and/or responses to scrutiny contain confidential information please ensure you have provided a version with this information redacted by 18 April 2024.

Ordinarily appeals are conducted on the basis of the appellants’ written appeal letters, and the material generated during the appraisal process. Use of additional written material is discouraged, and the panel cannot receive any new evidence. If, exceptionally, you feel there is written material that will not be before the panel that you would wish to rely on you must let the NICE Appeal team know by return of letter, indicating what the material is, why it is desirable to submit it, and when it will be available, by no later than 3 May 2024. Please note that the appeal panel cannot accept papers that are tabled late or ad hoc, as this affects the preparation of the panel and other parties for the appeal.

Yours sincerely

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Sharmila Nebhrajani OBE

Non-Executive Director & Chairman

National Institute for Health and Care Excellence