Sent by e-mail only: XXXXXXXXXXXXXX, XXXXXXXXXXXXXXX

FAO XX X XXXXX & XX X XXXXXXXXX

British Paediatric Neurology Association

2 St Andrews

Regent's Park

London

NW1 4LB

10 May 2024

Dear XX XXXXX and XX XXXXXXXX

**Re: Final Draft Guidance – Fenfluramine for treating seizures associated with Lennox-Gastaut Syndrome in people 2 years and over (ID1651)**

Thank you for your letter of 2 May 2024, lodging an appeal against the above Final Draft Guidance (FDG).

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.

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

**Appeal point 1(a).1: Large unmet need in patients with Lennox-Gastaut syndrome**

I am not minded to refer this appeal point to the Appeal Panel.

I note all that you say regarding the large unmet need in patients with Lennox-Gastaut syndrome. In order to refer an appeal point to the Appeal Panel for determination, however, I need to be satisfied that the Committee has arguably failed to act fairly. The fact of there being an unmet need does not, per se, meet that test. I invite the BPNA to explain in its response, how in your view, the Committee acted unfairly in reaching its negative recommendation. You may find it helpful to refer to NICE's Guide to the technology appraisal and HST appeal process, which explains in section 4.3 what is required under Ground 1(a), as follows:

*NICE is committed to following a fair process throughout the technology appraisal and highly specialised technologies process. An appellant who believes that an evaluation was not fair may appeal on this ground. This ground relates only to the fairness of the process followed and not to the content of the final draft guidance. It should be noted that if an appellant does not agree with final draft guidance this does not make it unfair. For example, although it is unfair to exclude relevant data from the technology appraisal and highly specialised technologies evaluation process, it is not unfair to consider the relevant data but then reach a view with which the appellant did not agree.*

*This ground of appeal does not cover an argument that it is 'unfair' in a general sense, for example, that it is 'unfair' to patients not to recommend a treatment.*

*Unspecific allegations of unfairness, for example, an alleged inability to understand a conclusion, will not be accepted as a valid appeal point. Details and evidence must be provided in every case.*

*NICE requires appellants to explain what steps they took to promptly resolve any unfairness when they first became aware of it. The appeal panel may interpret the absence of any such steps, without sufficient reason, as evidence that there was in fact no such unfairness, or potentially as a reason not to refer guidance back to the committee or to request changes to guidance.*

I also note with concern your statement that the BPNA "*was not given an opportunity to contribute to the discussions, despite repeated requests*".

NICE's Manual for health technology evaluations explains that NICE invites stakeholders including organisations representing healthcare professions to participate in technology evaluations. The BPNA was so invited and participated in this evaluation as a consultee. The Manual further explains (at 1.2.18 and 1.3.13) that professional organisations who are consultees should be invited to submit evidence and nominate clinical, patient and commissioning experts for the evaluation.

I invite you to provide further detail in your response to this letter as to whether and how in your view, NICE departed from the requirements of the Manual in the current evaluation.

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

**Appeal point 2.1: The Appraisal Committee’s refusal to recommend the use of fenfluramine for treatment of seizures in patients with Lennox-Gastaut syndrome cannot reasonably be justified in the light of the evidence submitted**

I am not minded to refer this appeal point to the Appeal Panel.

NICE's Guide to the technology appraisal and HST appeal process explains that "*NICE will not accept an appeal simply because a consultee disagrees with the views or conclusions in the FDG*". Rather, "*this ground means that the guidance is obviously and unarguably wrong, illogical, or 'does not add up'*. *The appeal panel will not make its own judgements about the technology, but it will review the committee's decisions to see if they can reasonably be justified, based on the evidence that was available to the committee.*"

My reading of appeal point 2.1 in your appeal letter is that you disagree with the Committee's conclusion, but that it does not support a view that the Committee's conclusion was arguably unreasonable. You say that "*overall, the evidence suggests that the efficacy and tolerability of fenfluramine is comparable to that of cannabidiol plus clobazam in treatment of seizures in patients with LGS, and … unlike cannabidiol, fenfluramine does not need co-administration of clobazam, which can have its own tolerability issues.*" These conclusions would not on their own be sufficient to drive a positive recommendation, in the absence of cost-effectiveness.

I note that you are concerned that the committee "*may have overlooked nearly 60% reduction during the clinical trial and nearly 50% during OLE in the frequency of tonic-clonic seizures.*" I believe this is considered in the Committee's papers for its meeting on 31 January 2024 – see point B3.3.3 on page 119. I would invite you to expand upon this point in your reply to this letter if, having considered this, you remain of the view that the committee's conclusion was unreasonable on the basis that this issue was overlooked or not properly considered.

Conclusion

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

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.

1. 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 3 June 2024.
2. 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 28 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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Dr Mark Chakravarty

Lead Non-Executive Director for Appeals & Vice Chairman

National Institute for Health and Care Excellence