NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Fenfluramine hydrochloride for treating Lennox-Gastaut seizures in people aged 2 and over

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of fenfluramine hydrochloride within its marketing authorisation for treating Lennox-Gastaut seizures in people aged 2 and over.

Background

Lennox-Gastaut syndrome is a severely debilitating form of epilepsy that begins in early childhood between the ages of 2 and 7 years. It is characterised by frequent seizures of different types. Drop seizures result in a loss of muscle tone or stiffening of muscles, and people can crash to the ground. This may result in severe injuries and hospitalisation. The condition is also associated with severe learning and behavioural disorders.[1]

The prevalence of Lennox-Gastaut syndrome in the UK is estimated at 5.8 per 100,000 people.[2] It accounts for 1-10% of childhood epilepsies and 1-2% of all epilepsies.[1] Approximately 5% of children with Lennox-Gastaut syndrome will die during childhood.[2]

Lennox-Gastaut syndrome is primarily manged with anti-epileptic drugs, and may be supported by a ketogenic diet or vagus nerve stimulation. However, the seizures are often resistant to treatment. NICE clinical guideline 217 recommends sodium valproate as a first-line treatment option, and if seizures are inadequately controlled, lamotrigine as a second-line monotherapy or add-on treatment. If second-line treatment is unsuccessful, clobazam, rufinamide, topiramate or cannabidiol in combination with clobazam (NICE Technology appraisal guidance 615) can be considered as add-on treatments.

The technology

Fenfluramine hydrochloride (Fintepla, Zogenix) does not currently have marketing authorisation in the UK for Lennox-Gastaut syndrome. It has been studied in clinical trials as adjunctive therapy for adults and children over the age of 2 with Lennox-Gastaut syndrome.

Fenfluramine hydrochloride does have marketing authorisation for the treatment of Dravet syndrome, which is another severe, lifelong and treatment-resistant form of epilepsy that begins in early childhood.

Intervention(s)	Fenfluramine hydrochloride
Population(s)	People aged 2 and over with Lennox-Gastaut syndrome whose seizures are inadequately controlled by established clinical management.

Comparators	Established clinical management without fenfluramine hydrochloride, which may include combinations of:
	• Anti-seizure medications, including but not limited to:
	  ○ cannabidiol with clobazam
	  ○ sodium valproate
	  ○ lamotrigine
	  ○ rufinamide
	  ○ topiramate
	  ○ felbamate
	  ○ clobazam
	• ketogenic diet
	• vagus nerve stimulation
	• surgery

Outcomes	The outcome measures to be considered include: • seizure frequency (overall and by seizure type) • proportion of people seizure-free (overall and by seizure type) • response rate (overall and by seizure type) • seizure severity • incidence of status epilepticus • mortality • adverse effects of treatment • health-related quality of life

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related Technology Appraisals:** Cannabidiol with clobazam for treating seizures associated with Lennox–Gastaut syndrome (2019). NICE Technology appraisal guidance 615 Cannabidiol for adjuvant treatment of seizures associated with Dravet syndrome (2019). NICE Technology appraisal guidance 614 Fenfluramine for treating seizures associated with Dravet syndrome (2022). NICE Technology appraisal guidance 808 **Related Guidelines:** Epilepsies in children, young people and adults (2022) NICE clinical guideline 217 **Related Quality Standards:** Quality standard for the epilepsies in adults (2013) NICE quality standard 26 Quality standard for the epilepsies in children and young people (2013) NICE quality standard 27

Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 119. Specialist neuroscience services for children. NHS England (2018) Service specification: Children's Epilepsy Surgery Service (CESS). Reference: E09/S/e

Questions for consultation

Which treatments are considered to be established clinical practice in the NHS for the treatment of Dravet syndrome?

Where do you consider fenfluramine hydrochloride will fit into the existing care pathway for Lennox-Gastaut syndrome, as described in NICE clinical guideline 217?

Will people with Lennox-Gastaut syndrome continue to use fenfluramine hydrochloride in adulthood?

Have all relevant comparators for fenfluramine hydrochloride been included in the scope?

Are the outcomes listed appropriate?

Would fenfluramine hydrochloride be a candidate for managed access?

Are there any subgroups of people in whom fenfluramine hydrochloride is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Is fenfluramine hydrochloride likely to require additional monitoring for the risk of adverse cardiovascular outcomes such as heart valve disease?

Do you consider that the use of fenfluramine hydrochloride can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which fenfluramine hydrochloride will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

NICE's health technology evaluations: the manual states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost-comparison methodology for this topic?

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1 Orphanet (undated) Lennox-Gastaut syndrome. Accessed September 2022

2 Chin RF, et al. (2021). Prevalence, healthcare resource utilization and mortality of Lennox-Gastaut syndrome: retrospective linkage cohort study. Seizure, 91, 159-166.