NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

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

Final scope

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 fall suddenly 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-seizure medication, 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, UCB Pharma) 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
	  ○ levetiracetam
	• 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 (patients and carers)

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

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.