NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Cannabidiol for adjuvant treatment of seizures associated with Lennox-Gastaut syndrome

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of cannabidiol within its marketing authorisation for adjuvant treatment of seizures associated with Lennox-Gastaut syndrome.

Background

Lennox-Gastaut syndrome is a severely debilitating form of generalised paediatric epilepsy that begins in early childhood between the ages of 2 and 7 years. It is characterised by tonic seizures, atypical absence seizures, drop seizures and slow mental development. The condition is also associated with behavioural disorders[1]. The incidence of Lennox-Gastaut syndrome is estimated at 2 per 100,000 children[1]. Lennox-Gastaut syndrome related mortality is estimated at around 5%, however the seizures are often resistant to treatment[2].

Lennox-Gastaut syndrome is primarily manged with anti-epileptic drugs, and may be supported by a ketogenic diet or vagus nerve stimulation. NICE clinical guideline 137 recommends sodium valproate or topiramate as first-line treatment options, and if seizures are inadequately controlled, clobazam or stiripentol are recommended as adjunctive treatment. For Lennox-Gastaut syndrome NICE clinical guideline 137 recommends sodium valproate as a first-line treatment option, and if seizures are inadequately controlled, lamotrigine as an adjunctive treatment. Further anti-epileptic drugs, including rufinamide, topiramate and felbamate may be considered by tertiary epilepsy specialists

The technology

Cannabidiol (Epidiolex, GW Pharma) is a small-molecule cannabinoid compound extracted from the *Cannabis sativa* plant. The precise mechanism of action of cannabidiol is unknown, although it is thought to act on the GPR55 and TRPV1 protein channels, which is expected to have an effect on epileptic activity in the brain. It is administered orally.

Cannabidiol does not currently have a marketing authorisation in the UK for Lennox-Gastaut syndrome. It has been studied in placebo controlled trials as an adjuvant treatment for inadequately controlled Lennox-Gastaut syndrome in people taking one or more anti-epileptic drugs.

Intervention(s)	Cannabidiol in addition to current clinical management
Population(s)	People with Lennox-Gastaut syndrome whose seizures are inadequately controlled by established clinical management.
Comparators	Established clinical management without cannabidiol, which may include combinations of: • sodium valproate • lamotrigine • rufinamide • topiramate • felbamate • clobazam • levetiracetam • ketogenic diet • vagus nerve stimulation
Outcomes	The outcome measures to be considered include: • seizure frequency (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.

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 and NICE Pathways	Related Technology Appraisals: None Appraisals in development (including suspended appraisals) Cannabidiol for adjuvant treatment of seizures associated with Dravet syndrome (ID1211) Fenfluramine for treating Dravet syndrome (ID1109) Related Guidelines: Epilepsies: diagnosis and management (2016) NICE clinical guideline 137. Review date 2018. 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 NICE Pathways: Epilepsy (2016) NICE pathway
Related National Policy	NHS England. Manual for prescribed specialised services 2016/17. Chapter 78. Neuropsychiatry services (adults and children) Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 2, 4 and 5.

References

1. Orphanet (undated) Lennox-Gastaut syndrome. Accessed 15 November 17)

2. Abu Saleh, T., & Stephen, L. (2008). Lennox gastaut syndrome, review of the literature and a case report. Head & Face Medicine, 4, 9.