NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Cannabidiol for treating seizures caused by tuberous sclerosis complex

Final scope

Final remit/appraisal objective

To appraise the clinical and cost effectiveness of cannabidiol within its marketing authorisation for treating seizures caused by tuberous sclerosis complex.

Background

Tuberous sclerosis or tuberous sclerosis complex is a rare genetic condition that causes mainly non-cancerous (benign) tumours to develop in different parts of the body. The tumours most often affect the brain, kidneys, heart, lungs, eyes and skin. Two disease causing genes have been identified: TSC1 and TSC2. Tuberous sclerosis is present from birth, although symptoms may not appear immediately. People with tuberous sclerosis complex present at different ages with a variety of clinical manifestations. The effect of tuberous sclerosis complex on the brain can cause epilepsy, a condition that causes seizures. Seizures can progress to become refractory, which is when the seizures no longer respond to anti-epileptic medication (also known as uncontrolled or intractable). In UK clinical practice, this means that 2 different anti-epileptic drugs have failed to control a person's seizures. Refractory epilepsy associated with tuberous sclerosis complex is associated with risks including sudden unexpected death in epilepsy, potentially fatal prolonged seizures (status epilepticus), and adverse impact on neurodevelopment.[1]

The estimated prevalence of tuberous sclerosis complex in the UK is 5.6 per 100,000.[2] Seizures are the most common presenting sign of tuberous sclerosis complex and occur in approximately 84% of people. The proportion of patients with tuberous sclerosis-related refractory epilepsy varies depending on the evidence source between 36% and 63%.[4] Based on this, the estimated number of people with tuberous sclerosis-related refractory epilepsy in the UK is 1555.[5]

Although there is no curative treatment for tuberous sclerosis, current treatment can help to manage symptoms. Anti-seizure medications such as vigabatrin are administered to control seizures. Everolimus may also be used to reduce the frequency of seizures, which are closely linked to issues with development in infants and children. Early management is important in preventing and reducing the cognitive, neurological and psychiatric consequences for people with tuberous sclerosis complex.

The technology

Cannabidiol (Epidyolex, 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 has a marketing authorisation in the UK as adjunctive therapy for treating seizures associated with TSC for patients 2 years of age and older.

Intervention(s)	Cannabidiol in addition to current clinical management
Population(s)	People with tuberous sclerosis complex whose seizures are inadequately controlled by established clinical management
Comparators	Established clinical management without cannabidiol, such as: • Anti-seizure medications • Everolimus • Vagus nerve stimulation • Ketogenic diet • Surgical resection
Outcomes	The outcome measures to be considered include: • change in frequency of seizures • response to treatment • 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:** 'Cannabidiol with clobazam for treating seizures associated with Dravet syndrome' (2019). NICE Technology Appraisal 614. Review date December 2022. 'Cannabidiol with clobazam for treating seizures associated with Lennox-Gastaut syndrome' (2019). NICE Technology

	Appraisal 615. Review date December 2022. **Related Guidelines:** 'Epilepsies: diagnosis and management' (2012). NICE guideline CG137. Updated 2021. **Guidelines in development:** 'Epilepsies in adults: diagnosis and management update'. Publication date to be confirmed. 'Epilepsies in children: diagnosis and management'. Publication expected April 2022. **Related Interventional Procedures:** 'Deep brain stimulation for refractory epilepsy in adults' (2020). NICE interventional procedures guidance 678. 'MRI-guided laser interstitial thermal therapy for drug-resistant epilepsy' (2020). NICE interventional procedures guidance 671. **Related Quality Standards:** 'Epilepsy in adults' (2013). NICE quality standard 26. 'Epilepsy in children and young people' (2013). NICE quality standard 27. **Related NICE Pathways:** Epilepsy (2012) NICE pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1-3. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 Everolimus for refractory focal onset seizures associated with tuberous sclerosis complex (ages 2 years and above) NHS England.

References

1 Laxer et al. (2014) The consequences of refractory epilepsy and its treatment. Epilepsy & Behaviour. 37: 59-70.

2 Hallet L, Foster T, Liu Z et al. (2011) Burden of diseases and unmet needs in tuberous sclerosis complex with neurological manifestations: systematic review. Current Medical Research and Opinion. 27: 1571-1583.

3 Kingswood JC, d'Augeres GB, Belousova E et al. (2017) Tuberous sclerosis registry to increase disease awareness (TOSCA) – baseline data on 2093 patients. Orphanet Journal of Rare Diseases. 12(2): 1-13.

4 Chu-Shore CJ, Major P, Camposano S et al. (2010) The natural history of epilepsy in tuberous sclerosis complex. Epilepsia. 51(7): 1236-1241.

5 Office for National Statistics (2020) Population estimates for the UK, England and Wales, Scotland and Northern Ireland: mid-2019.