NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Perampanel for adjunctive treatment of partial onset or generalised tonic-clonic seizures in children aged below 12 years with epilepsy

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of perampanel within its marketing authorisation for adjunctive treatment of partial onset or generalised tonic-clonic seizures in children with epilepsy.

Background

Epilepsy is a neurological condition characterised by recurrent seizures unprovoked by any immediately identifiable cause. An epileptic seizure is a sudden episode with changes in movement, sensation, behaviour, emotion, memory or consciousness due to abnormal signalling between the nerve cells in the brain. Epilepsy is not a uniform condition, but comprises many different seizure types and epilepsy syndromes. The severity of the condition and the prognosis vary according to the type of epilepsy.

Epileptic seizures can be broadly categorised into 2 main types: partial and generalised. In partial seizures (also known as focal seizures) the abnormal signalling begins in, or is restricted to, a localised part of the brain. Generalised seizures are characterised by more widespread signalling involving both hemispheres of the brain at the same time. Partial seizures may become secondarily generalised seizures if the abnormal signalling spreads to involve the entire brain. The symptoms of a partial seizure include strange sensations and random bodily behaviour, and the person may not remember what has happened after the seizure has passed. Symptoms of generalised seizures include sudden stiffening or relaxing of the muscles which may mean the person falls over, twitching arms and legs, and loss of consciousness.

Epilepsy is the most common neurological condition in the UK. It has been estimated to affect between 362,000 and 415,000 people in England[1]. Annually, there are approximately 50 new cases of people presenting with epilepsy per 100,000 population. People with epilepsy have a 2 to 3 times higher overall risk of dying than the general population[2].

For focal seizures, NICE clinical guideline 137 (NG137) 'Epilepsies: diagnosis and management' recommends carbamazepine or lamotrigine as first line antiepileptic drugs (AED), and levetiracetam, oxcarbazepine or sodium valproate if carbamazepine and lamotrigine are unsuitable or not tolerated. If the first AED tried is ineffective, an alternative from these 5 AEDs is recommended. Adjunctive treatment is considered if a second well-tolerated

AED is ineffective. NG137 recommends carbamazepine, clobazam, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, sodium valproate or topiramate as adjunctive therapies.

For generalised tonic clonic seizures, NG137 recommends sodium valproate as first-line treatment and lamotrigine, carbamazepine or oxcarbazepine if sodium valproate is unsuitable. If first-line treatments are ineffective or not tolerated, adjunctive treatments are clobazam, lamotrigine, levetiracetam, sodium valproate and topiramate.

The technology

Perampanel (Fycompa, Eisai) is an antagonist of the AMPA receptor (a type of glutamate receptor that participates in excitatory neurotransmission). Glutamate is the main stimulatory neurotransmitter in nerve cells which in the context of epilepsy can trigger and maintain seizures. It is administered orally.

Perampanel does not currently have a marketing authorisation in the UK for treating epileptic seizures in children aged up to 12 years. It has been studied in a non-randomised single arm clinical trial as adjunctive therapy in children aged 4 to 12 years with inadequately controlled partial onset or primary generalised tonic-clonic seizures, who were on a stable dose of 1 to 3 antiepileptic drugs

Perampanel has a marketing authorisation for the following related indications in adults and adolescents from 12 years of age: adjunctive treatment of partial-onset seizures with or without secondarily generalised seizures, and adjunctive treatment of primary generalised tonic-clonic seizures in idiopathic generalised epilepsy.

Intervention	Perampanel adjunctive therapy
Populations	Children aged below 12 years with: • uncontrolled partial onset seizures with or without secondary generalisation • uncontrolled primary generalised tonic-clonic seizures
Comparators	Other adjunctive therapies, including: • For people with uncontrolled partial onset seizures: carbamazepine, clobazam, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, sodium valproate and topiramate • For people with uncontrolled generalised tonic-clonic seizures: clobazam, lamotrigine, levetiracetam, sodium valproate and topiramate

Outcomes	The outcome measures to be considered include: • change in seizure frequency • seizure free rate • time to first seizure • response rate • seizure severity • 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 Guidelines: 'Epilepsies: diagnosis and management' (2012) NICE guideline CG137. In process of being updated. Guidelines in development 'Epilepsies in children: diagnosis and management' Publication expected April 2021. 'Epilepsies in adults: diagnosis and management update' Publication expected January 2021. Related NICE Pathways: Epilepsy (2019) NICE pathway http://pathways.nice.org.uk/
Related National	The NHS Long Term Plan, 2019. NHS Long Term Plan

Policy	NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019): Chapter 78. Neuropsychiatry services (adults and children) NHS England (2018) Children's Epilepsy Surgery Service (CESS) - Service Specification. Ref: E09/S/e NHS England (2018) Clinical Commissioning Policy: Deep Brain Stimulation for Refractory Epilepsy Ref: 07603 Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains1, 2 and 4. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Is the population defined appropriately? Would there be value in extending the population to include people aged 12 years and over, for whom perampanel already has a marketing authorisation?

Have all relevant comparators for perampanel been included in the scope?

Which adjunctive treatments are considered to be established clinical practice in the NHS for uncontrolled partial onset seizures with or without secondary generalisation?

Which adjunctive treatments are established clinical practice in the NHS for uncontrolled primary generalised tonic-clonic seizures?

Would perampanel be given in combination with any other adjunctive treatments or replace other adjunctive treatments?

Are the outcomes listed appropriate?

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

Where do you consider perampanel will fit into the existing NICE pathway, Epilepsy?

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 perampanel 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.

Do you consider perampanel to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of perampanel can result in any potential significant and 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 Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1 NICE guideline CG137 (2012) 'Epilepsies: diagnosis and management'. https://www.nice.org.uk/guidance/cg137/chapter/Introduction

2 Keezer MR, Bell GS, Neligan A et al. (2016) Cause of death and predictors of mortality in a community-based cohort of people with epilepsy. Neurology Feb 2016, 86 (8) 704-712. DOI: https://doi.org/10.1212/WNL.0000000000002390