Epilepsies in children, young people and adults

[Q] Effectiveness of antiseizure medications for self-limited epilepsy with centrotemporal spikes

NICE guideline NG217

Evidence reviews underpinning recommendations 6.4.1-6.4.8 in the NICE guideline

April 2022, updated 2026

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ISBN: 978-1-4731-4513-9

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Update 2026

This evidence review and accompanying recommendations 6.4.2 to 6.4.4 were updated following the UK licencing of sultiame in January 2025. An expert working group (EWG) was formed to agree any changes to the current recommendations. The rationale supporting the revised recommendations is included below in the committee discussion. No new evidence was identified to inform these changes.

Review question

What antiseizure medications (monotherapy or add-on) are effective in the treatment of self-limited epilepsy with centrotemporal spikes?

Introduction

Self-limited epilepsy with centrotemporal spikes (SeLECTS) is a common focal epilepsy in childhood in which there may be infrequent seizures. Children grow out of this epilepsy by early teenage years; therefore, one of the main considerations is whether to treat the child with antiseizure medications (ASMs). Understanding the effectiveness and the potential adverse effects is important in clinical practice, and to inform discussions and decisions with families. The aim of this review is to determine which ASMs improve outcomes in those with SeLECTS.

Summary of the protocol

Please see Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	Children and young people with confirmed self-limited epilepsy with centrotemporal spikes
Intervention	The following ASMs and their combinations will be considered: • Carbamazepine • Clobazam • Gabapentin • Lacosamide • Levetiracetam • Oxcarbazepine • Sodium Valproate • Sultiame

	• Topiramate • Lamotrigine • Zonisamide
Comparison	• Any of the above and their combinations • No treatment/placebo
Outcomes	**Critical** • Seizure freedom (12 months data and short term [minimum 3 months with 100% freedom] of starting treatment) • Reduction of seizure frequency >50% • Time to withdrawal of treatment or change of medication (for example, because of uncontrollable seizures) • Side effects, as assessed by: o % of patients with reported side effects (trial defined adverse and serious adverse effects) o treatment cessation due to adverse event [dichotomous outcome only]) **Important** • Neuropsychological changes (IQ testing, or other validated tools) • Social functioning changes (behaviour reported by parents/caregivers/school or validated tools) • EEG outcomes (ESES, CSWS or spike wave index)

ASMs: antiseizure medications; CSWS: continuous spike-wave of slow-wave sleep; ESES: electrical status epilepticus in sleep; EEG: electroencephalogram; IQ: intelligence quotient

When this review was originally conducted, the name of the epilepsy syndrome used in the searches and the review was childhood epilepsy with centrotemporal spikes (CECTS) and benign epilepsy with centrotemporal spikes (BEBCTS), however the name of this epilepsy syndrome changed during guideline development to self-limited epilepsy with centrotemporal spikes (SeLECTS), and amendments to reflect this change were done as appropriate throughout this report.

For further details see the review protocol in appendix A.

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document (supplementary document 1). Declarations of interest were recorded according to NICE's conflicts of interest policy.

Clinical evidence

Included studies

Nine studies reporting on 8 randomised controlled trials (RCTs) were identified for inclusion in this review (Ahadi 2020, Borggraefe 2013, Coppola 2007, Kang 2007, Kwon 2013, Mitsudame 1997, Rating 2000, Suo 2021, Tacke 2018); 2 of these provided data from the same study (Borggraefe 2013, Tacke 2018).

Two studies compared levetiracetam (LEV) to sultiame (STM) (Borggraefe 2013, Tacke 2018), 2 studies compared LEV to oxcarbazepine (OXC) (Coppola 2007, Suo 2021), 1 study compared LEV to carbamazepine (CBZ), 1 study compared topir-

amate (TPM) to CBZ (Kang 2007), 1 study compared clonazepam (CZP) to valproate (VAL) and CBZ (Mitsudame 1997), 1 study compared STM to placebo (Rating 2000) and 1 study compared OXC to no treatment.

Update 2026

An update search was completed but no new studies were identified.

The included studies are summarised from Table 2 to Table 7.

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies not included in this review with reasons for their exclusions are provided in appendix K.

Update 2026

136 studies were identified in the update search of which 3 studies were excluded (Cheng 2022, Feng 2024 and Liu 2024). These studies were added to the excluded studies table with reasons for their exclusion in appendix K.

Summary of clinical studies included in the evidence review

Summaries of the studies that were included in this review are presented from Table 2 to Table 7.

Table 2: Summary of included studies. Comparison 1: levetiracetam versus carbamazepine

Study	Population	Intervention	Comparison	Outcomes
Ahadi 2020 RCT Iran	N=92 children with a clinical diagnosis of benign childhood epilepsy with centro temporal spikes and an EEG showing characteristics of rolandic epilepsy Age, years, mean (SD): levetiracetam 8.7 (2.76);	Levetiracetam n=46 Levebel (levetiracetam) oral solution 100 mg/ml at initial dose of 25-30 mg/kg/day.	Carbamazepine n=46 Tegretol (carbamazepine) syrup 20 mg/ml at initial dose of 15-20 mg/kg/day.	• Seizure freedom • Side effects

Study	Population	Intervention	Comparison	Outcomes
	carbamaze-pine 8.36 (2.25), p=0.514.			

EEG: electroencephalogram; kg: kilogram; mg: milligram; ml: millilitre; RCT: randomised controlled trial; SD: standard deviation

Table 3: Summary of included studies. Comparison 2: levetiracetam versus sultiame

Study	Population	Intervention	Comparison	Outcomes
Borggraefe 2013 Multi-centre double blind RCT Germany	N = 44 children with benign epilepsy with centrotemporal spikes Mean age LEV: 8.7 years (SD 1.7) STM: 9.0 years (SD 1.5)	Levetiracetam (LEV) n=21 Starting dose: 10mg/kg Final dose: 30mg/kg Down dosing to 20mg/kg was permitted in case of AE	Sultiame (STM) n=22 Starting dose:2mg/kg Final dose: 6mg/kg Down dosing to 4mg/kg was permitted in case of AEs	• Seizure freedom (study defined treatment failure as occurrence of a seizure in 24 weeks) • Serious events leading to treatment withdrawal
Tacke 2018 Multi-centre double blind RCT Germany	See Borggraefe 2013	See Borggraefe 2013	See Borggraefe 2013	• Absence of rolandic discharge on EEG

AEs: adverse events; EEG: electroencephalogram; RCT: randomised controlled trial; SD: standard deviation

Table 4: Summary of included studies. Comparison 3: levetiracetam versus oxcarbazepine

Study	Population	Intervention	Comparison	Outcomes
Coppola 2007 Open label pilot RCT Italy	N = 39 children with benign epilepsy with centrotemporal spikes Mean age LEV: 10.5 years OXC: 8.4 years	Levetiracetam (LEV) n=21 Starting dose of 5mg/kg Final dose of 20mg/kg	Oxcarbazepine (OXC) n=18 Starting dose of 5mg/kg Final dose of 20mg/kg	• Seizure freedom (number of participants free from seizures at 18 months) • Adverse events leading to withdrawal • Adverse events (total AEs recorded, excluding those leading to withdrawal)
Suo 2021	N=70 children with benign epi-	Levetiracetam n=35 (n=32 included in final analysis)	Oxcarbazepine (OXC) n=35 (n=32 included	• Seizure freedom • Normalisation of

Study	Population	Intervention	Comparison	Outcomes
RCT China	lepsy with centrotem-poral spikes (n=64 in-cluded in final analy-sis) Age, years: Intervention group 8.47 ± 2.13; con-trol group 8.62 ± 2.21, Age at on-set, years: Intervention group 6.98 ± 1.82; con-trol group 7.13 ± 1.75	250 mg tablets (Keppra). Initial dose set at 10 mg/kg/day. Dose increased once every 7 days and maintained at 20–60 mg/kg/day.	in final analysis) 150 mg tablets. Initial dose set at 8–10 mg/kg/day, orally administered twice a day at an interval of 12 hours. Dose in-creased to 5–10 mg/kg/day every 5–7 days and maintained at 20–46 mg/kg/day.	EEG • Adverse events

AEs: adverse events; RCT: randomised controlled trial

Table 5: Summary of included studies. Comparison 4: topiramate versus carbamazepine

Study	Population	Intervention	Comparison	Outcomes
Kang 2007 Multi-centre, open label RCT Korea	N = 112 children with benign epilepsy with cen-trotemporal spikes Mean age TPM: 8.7 years (SD 1.9) CBZ: 8.7 years (SD 2.0)	Topiramate (TPM) n=58 Starting dose: 12.5mg/day Final dose of at least 50mg/day if weighed <30kg, or at least 75mg/day if weighed >30kg	Carbamazepine (CBZ) n=54 Starting dose: 10mg/kg/day Final dose of at least 20/kg/day	• Seizure freedom (number of partici-pant free of seizures over 28 weeks) • Adverse events (total AEs recorded, ex-cluding those which led to withdrawal) • Adverse events lead-ing to withdrawal

AEs: adverse events; RCT: randomised controlled trial

Table 6: Summary of included studies. Comparison 5, 6, and 7: clonazepam versus valproate/ carbamazepine

Study	Population	Intervention	Comparison	Outcomes
Mitsudome 1997 RCT Japan	N = 40 children with benign epilepsy with cen-trotemporal spikes	Clonazepam (CZP) n=20 Dose: 0.35-1.0mg/day	Valproate (VPA) n=10 Dose: 250-600mg/day	• EEG (disappearance of RD)

Study	Population	Intervention	Comparison	Outcomes
	Mean age CZP: 7.3 years (range 3.11- 9.11) VPA: 8.6 years (range 4.0 – 10.11) CBZ: 8.6 years (range 5.5 – 10.3)		Carbamazepine (CBZ) n= 10 Dose: 100-200mg/day	

AEs: adverse events; EEG: electroencephalogram; RCT: randomised controlled trial; RD: rolandic discharge

Table 7: Summary of included studies. Comparison 8: sultiame versus placebo

Study	Population	Intervention	Comparison	Outcomes
Rating 2000 Double blind RCT Germany	N = 66 children with with benign childhood epilepsy with centrotemporal spikes Mean age STM: 8 years (range 3-10) Placebo: 8 years (range 3-10)	Sultiame (STM) n=31 5mg/kg/day (in 3 administrations per day)	Placebo n=35	• Seizure freedom (defined as treatment failure, no seizure in first 7 days, no AEs or withdrawal) • EEG reading (defined as specific pathology)

EEG: electroencephalogram; RCT: randomised controlled trial

Table 8: Summary of included studies. Comparison 9: Oxcarbazepine versus no treatment

Study	Population	Intervention	Comparison	Outcomes
Kwon 2013 RCT South Korea	N=39 children with newly diagnosed benign partial epilepsy Age, mean, years: intervention group 8.2	Oxcarbazepine n=13 Initially administered once or twice a day at a dose of 5-10 mg/kg/day and titrated to 10-20 mg/kg/day over a week.	No treatment n=16	• Seizure frequency • Reduction of seizure frequency >50% • Normalisation of sleep EEG • EEG spike index • Full-scale intelligence quotient

Study	Population	Intervention	Comparison	Outcomes
	±2.3; control group 8.5±2.3.			

EEG: electroencephalogram; RCT: randomised controlled trial; SD: standard deviation

See the full evidence tables in appendix D. No meta-analysis was conducted (and so there are no forest plots in appendix E).

Summary of the evidence

Across all the comparisons identified in this review, the majority showed no important difference between the interventions compared (for example, levetiracetam versus sultiame, levetiracetam versus oxcarbazepine, topiramate versus carbamazepine or valproate versus carbamazepine). Exceptions included clonazepam versus valproate, and clonazepam versus carbamazepine, where clonazepam had an important benefit in terms of outcome rolandic discharge on electroencephalogram (EEG), and sultiame versus placebo, where sultiame had an important benefit in terms of outcome treatment failure.

Typically, the comparisons where no difference in outcomes between interventions was found included less participants and had very serious imprecision, therefore they should not be taken as definitive evidence of no difference between the interventions. There were also a number of outcomes in the protocol that were not reported on by any studies, including neuropsychological and social functioning changes. For the comparison of sultiame versus placebo, the findings were precise and high certainty therefore this is indicative that the true effect size is similar to the estimated effect reported by the study.

See appendix F for full GRADE tables.

Certainty of evidence included in the evidence review

See the clinical evidence profiles in appendix F.

Economic evidence

Included studies

A single economic search was undertaken for all topics included in the scope of this guideline, but no economic studies were identified which were applicable to this review question. See the literature search strategy in appendix B and economic study selection flowchart in appendix G.

As part of the 2026 an updated search was undertaken to identify published economic evaluations relevant to this review question. See the economic review protocol in appendix A and the literature search strategy in appendix B.

Excluded studies

A single economic search was undertaken for all topics included in the scope of this guideline. Please see appendix B for details.

From the 2026 updated search for this review question no economic studies were reviewed at the full text and excluded from this review.

Summary of studies included in the economic evidence review

No economic evidence was identified which was applicable to this review question.

Economic model

No economic modelling was undertaken for this review given the paucity of identified evidence and the expectation there was unlikely to be a significant resource impact from recommendations.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

As the seizures associated with SeLECTS often stop around the age of puberty, it is not clear whether it is necessary to prescribe ASMs to all children who present with this condition. The committee therefore agreed that seizure freedom and reduction in seizure frequency should be included as critical outcomes for this review to evaluate the effectiveness of antiseizure medications for this condition. However, as there is a risk of side effects the committee agreed that time to withdrawal of treatment and adverse events should also be included as critical outcomes.

Neuropsychological changes and social functioning changes were included as important outcomes as deterioration in these areas could indicate progression to a different form of epilepsy or an adverse reaction to treatment. EEG readings were also included as an important outcome as changes on these can also indicate progression of the condition and there is a risk that certain medications may exacerbate abnormal features seen on EEG.

Certainty of evidence

The quality of the evidence for this review was assessed using GRADE methodology. The majority of outcomes were considered very low or low quality indicating high uncertainly in the reliability of the data. Data was generally downgraded due to risk of bias, methods were poorly reported, specifically in regard to the randomisation processes and measurement of outcomes. Data was also downgraded due to imprecision. Studies only included a small number of participants; therefore, overall the data should be regarded with some caution.

Benefits and harms

Self-limited epilepsy with centrotemporal spikes is an age-related epilepsy syndrome which subsides by early teenage years. Seizures can be infrequent and confined to sleep with limited impact on the child's well-being which means the main decision is whether to treat with ASMs. The committee agreed the decision should be individually tailored following discussion between the clinician, the child and their parent/carer on the risks and benefits of treatment and non-treatment. For some children, seizures can be frequent and severe with effects on well-being and daily function, and risk injury or death. The committee stated that death is very rare, and the discussion should not cause undue worry to the child or parent/carer. Some children will have infrequent seizures, and therefore the side effects of daily therapy may be more detrimental to the child than the epilepsy itself.

The committee agreed that, if antiseizure medications are started in self-limited epilepsy with centrotemporal spikes, there should be a discussion with the person, their family and carers, if appropriate, about an individualised antiseizure medication strategy according to their epilepsy syndrome, treatment goals and the preferences of the person and their family or carers as appropriate. Treatment plans should be regularly reassessed, and its agreement should include a transparent explanation of the epilepsy syndrome, severity and duration of adverse effects that the person with epilepsy may experience and how should these be managed. The person, their family and carers, should also be made aware that they should be taking the least amount of medicines as possible to be effective due to the side effects of being on numerous medications.

The committee agreed that, overall, the evidence was limited and insufficient to make firm recommendations; therefore, they also relied on clinical experience and knowledge as well as on the existing evidence in evidence report E for focal seizures. The committee considered it was appropriate to extrapolate from this population as focal seizures are common in self-limited epilepsy with centrotemporal spikes. On this basis, the committee agreed that lamotrigine and levetiracetam should be considered as first-line treatment. There was high quality evidence that lamotrigine and levetiracetam were most effective in increasing the time to treatment withdrawal and, in particular, time to treatment withdrawal due to adverse events, suggesting these were better tolerated and more effective than other options. As second-line treatment, carbamazepine, oxcarbazepine and zonisamide were recommended as these appeared to be the next most effective. The precise choice between these options will be dependent on the preferences and the circumstances of the person being treated.

The Rating 2000 study was considered to be at low risk of bias, and this study showed sultiame was superior to placebo for reducing seizures; however, since this treatment is not licenced in the UK, it is difficult to recommend this as a first line therapy. As such, the committee agreed that prescription of sultiame as an add-on or alternative treatment should only be undertaken in discussion with a tertiary paediatric neurologist, to ensure that sultiame is not widely over-prescribed. The committee also questioned whether other drugs would show the same performance as sultiame if they had been tested in the same way.

The committee emphasised that, monotherapy should be used in the first instance. When starting alternative antiseizure medications, the dose of the new antiseizure medication should be slowly increased, whilst the existing antiseizure medication is tapered off. When starting add-on antiseizure medications, the additional antiseizure medication should be carefully titrated, in line with the BNF guidance, adverse events monitored, and there should be a frequent treatment review.

The evidence did not provide data on all treatments which are currently available, therefore making recommendations on specific antiseizure medications was difficult. The committee agreed that, in their experience, carbamazepine, oxcarbazepine and lamotrigine may rarely lead to increased seizures and/or the evolution to another epilepsy syndrome with greater effects on cognitive function.

The committee also agreed that if there is concern regarding school performance, advice should be sought from an epilepsy specialist. School performance is a good indicator of cognition since it reflects performance both in processing and retention of information. If any deterioration is noted, an EEG should be performed to exclude electrical status epilepticus in sleep (ESES)/ continuous spike-wave of slow-wave sleep (CSWS). A neuropsychology assessment to review academic performance should also be performed.

As noted previously, this is an age-related condition and therefore consideration should be given to the timing of discontinuation of treatment. When the child has been free of seizures for 2 years, discontinuation of treatment can be considered. The committee agreed that seizures will generally stop by early teenage years; if treatment has not already ceased, then it should be discontinued when the child reaches 14.

The committee were not surprised that in an epilepsy syndrome in which seizures may be infrequent and, only at night, there were a limited number of studies. Although evidence is scarce, the committee did not prioritise this topic for a research recommendation as they were able to base the recommendations for first- and second-line treatment on the evidence for treating focal seizures.

Update 2026

In January 2025, sutiame was licenced in the UK for the use in children and young people for the treatment of benign childhood epilepsy with centrotemporal spikes. An expert working group (EWG) was formed to consider whether any changes were required to the current recommendation for sultiame. Recommendations from the guideline had been to consider sultiame as a third line option mainly due to the lack of licencing at the time of the guideline publication.

An update search did not identify any new evidence and the EWG discussed the existing evidence on sultiame. High certainty evidence (Rating 2000) suggested a clinically important benefit for sultiame for treatment failure compared to placebo. Very low certainty evidence (Borggraefe 2013) showed no difference between sultiame and levetiracetam for the outcome's treatment failure and adverse events. The EWG agreed that sultiame should be considered as a second line monotherapy treatment option as the evidence showed a benefit over placebo and no difference against levetiracetam which is recommended as a first line option.

Sultiame was not recommended as a first line option as the evidence was limited to two small studies with high number of dropouts. Comparatively the other recommended treatments were based on the larger evidence base for focal seizures (see Evidence report E). The second line treatments were listed alphabetically as there was no evidence that one treatment was better than the others. The EWG were aware of a suggested link between sultiame and reduced cognition and were cautious to recommend as a first line option. However, sultiame has widespread use in Europe (including Germany) where it is well tolerated by children.

The EWG reviewed the Summary of Product Characteristics (SPC) for sultiame and understood that the licence states that treatment should only be conducted by paediatric neurologist with sufficient experience in treating epilepsy. The EWG discussed that this terminology of licencing would be applicable to use in Germany but not compatible with the UK model of care for epilepsy. There are fewer paediatric neurologists in the UK compared to Germany and most patients would be treated by a paediatrician with expertise in epilepsy. If prescribing was limited to a paediatric neurologist this would widen the already existing equality issues for children's access to medicines. It was agreed to amend the prescribing footnote from paediatric neurologist to paediatric epilepsy specialist in line with other recommendations in this guideline and the current model of care in the UK.

Cost effectiveness and resource use

A systematic review of the economic literature was conducted but no relevant studies were identified which were applicable to this review question.

The committee did not make any recommendations which changed current practice. Therefore, there will not be any impact upon resource use.

Update 2026

Sultiame medication costs are 3 times higher than the next most costly second line treatment zonisamide. There is some uncertainty around the cost of sultiame as the medication is currently imported and licensure in the UK may lead to changes in prices. The cost only includes those associated with purchasing the medicine. Sultiame may be the optimal treatment for some individuals either because it leads to reduced seizures or a more tolerable adverse event profile. A reduction in resource use (for example through reduced seizures or emergency hospital admissions) could be achieved in these individuals.

Sultiame is currently used in the NHS and moving it from third to second line is likely to only lead to a small if any increase in resource use given the small population size, limited time for which the medication is prescribed and that other treatments are first line. Reduction in resource use and quicker access to treatment may also be achieved through changing the need for a tertiary paediatric neurologist consultation to one with a paediatric epilepsy specialist.

Other factors the committee took into account

The committee noted that, in line with the BNF, clinicians should be aware of the risks of serious complications associated with carbamazepine and potentially medicines with a similar chemical structure (such as oxcarbazepine) for people of Han Chinese, Thai, European or Japanese family background. In addition, in line with the MHRA, the committee emphasised that long-term treatment with carbamazepine can cause decreased bone mineral density and increased risk of osteomalacia. The committee noted that appropriate supplementation should be considered for those at risk.

Recommendations supported by this evidence review

This evidence review supports recommendations 6.4.1-6.4.8.

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Appendices

Appendix A – Review protocols

Review protocol for review question: What antiseizure medications (monotherapy or add-on) are effective in the treatment of self-limited epilepsy with centrotemporal spikes?

Table 9: Review protocol

Field	Content
PROSPERO registration number	CRD42019146620
Review title	Effectiveness of ASMs for self-limited epilepsy with centrotemporal spikes (SeLECTS)
Review question	What ASMs (individually or in combination) are effective in the treatment of seizures in self-limited epilepsy with centrotemporal spikes?
Objective	The objective of this review is to determine which antiseizure medications (ASMs) improve outcomes in those with self-limited epilepsy with centrotemporal spikes. This review will determine the effectiveness of drugs given alone or in combination.
Searches	The following databases will be searched: • CDSR • CENTRAL • DARE • HTA • MEDLINE & MEDLINE In-Process and Other Non-Indexed Citations • Embase • EMCare Searches will be restricted by:

Field	Content
	• Date: No date limit • English language studies • Human studies • RCT and systematic review study design filter
Condition or domain being studied	Self-limited epilepsy with centrotemporal spikes (SeLECTS)
Population	Inclusion: children and young people with confirmed self-limited epilepsy with centrotemporal spikes
Intervention/Exposure/Test	The following ASMs and their combinations will be considered: • Carbamazepine • Clobazam • Gabapentin • Lacosamide • Levetiracetam • Oxcarbazepine • Sodium Valproate • Sultiame • Topiramate • Lamotrigine • Zonisamide
Comparator/Reference standard/Confounding factors	• Any of the above and their combinations • No treatment/placebo
Types of study to be included	• Systematic review of RCTs • RCTs
Other exclusion criteria	• Studies with a mixed population (this is, including children and young people with epilepsy and others with a condition different to epilepsy) will be excluded, unless subgroup analysis for epilepsy has been reported • Studies with a mixed population (this is, including children, and young people with SeLECTS and other types of epilepsy) will be excluded, unless subgroup analysis for epilepsy with SeLECTS has been reported

Field	Content
	• Conference abstracts will be excluded because these do not typically provide sufficient information to fully assess risk of bias
Context	Recommendations will apply to those receiving care in any healthcare settings (for example, community, primary, secondary care)
Primary outcomes (critical outcomes)	• Seizure freedom (12 months data and short term [minimum 3 months with 100% freedom] of starting treatment). *Due to anticipated heterogeneity in reporting of seizure freedom, data will be extracted as presented within included studies. Where a study reports multiple variants then all data will be extracted. For decision making priority will be given to data presented as "time to 12 months seizure freedom", (this is, time to event: HR or mean time) followed by "achievement of 12 months seizure freedom" (RR). Minimum follow up data of 3 months will be included.* • Reduction of seizure frequency >50% • Time to withdrawal of treatment or change of medication (for example, because of uncontrollable seizures) • Side effects, as assessed by: ○ % of patients with reported side effects (trial defined adverse and serious adverse effects) ○ treatment cessation due to adverse event (dichotomous outcome only) Outcomes are in line with those described in the core outcome set for epilepsy http://www.cometinitiative.org/studies/searchresults
Secondary outcomes (important outcomes)	• Neuropsychological changes (IQ testing, or other validated tools) • Social functioning changes (behaviour reported by parents/caregivers/school or validated tools) • EEG outcomes (ESES, CSWS, or spike wave index)
Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into STAR and de-duplicated. Titles and abstracts of the retrieved citations will be screened to identify studies that potentially meet the inclusion criteria outlined in the review protocol. Duplicate screening will not be undertaken for this question. Full versions of the selected studies will be obtained for assessment. Studies that fail to meet the inclusion criteria once the full version has been checked will be excluded at this stage. Each study excluded after checking the full version will be listed, along with the reason for its exclusion. A standardised form will be used to extract data from studies. One reviewer will extract relevant data into a standardised

Field	Content
	form, and this will be quality assessed by a senior reviewer.
Risk of bias (quality) assessment	Quality assessment of individual studies will be performed using the following checklists: • ROBIS tool for systematic reviews • Cochrane RoB tool v.2 for RCTs The quality assessment will be performed by one reviewer and this will be quality assessed by a senior reviewer.
Strategy for data synthesis	Depending on the availability of the evidence, the findings will be summarised narratively or quantitatively. <u>Data synthesis</u> Where possible pairwise meta-analyses will be conducted using Cochrane Review Manager software. A fixed effect meta-analysis will be conducted and data will be presented as risk ratios for dichotomous outcomes. Peto odds ratio will be used for outcomes with zero events in one arm. Mean differences or standardised mean differences will be presented for continuous outcomes. <u>Heterogeneity</u> Heterogeneity in the effect estimates of the individual studies will be assessed using the I^2 statistic. I^2 values of greater than 50% and 75% will be considered as significant and very significant heterogeneity, respectively. In the presence of heterogeneity, sub-group analysis will be conducted: • according to the risk of bias of individual studies • those with and without learning disabilities • by age (older people/adults/children) • study location Exact sub-group analysis may vary depending on differences identified within included studies. If heterogeneity cannot be explained using these methods, random effects model will be used. If heterogeneity remains above 75% and cannot be explained by sub-group analysis; reviewers will consider if meta-analysis is appropriate given characteristics of included studies. <u>Minimal important differences (MIDs):</u> • Default MIDs will be used for risk ratios and continuous outcomes only, unless the committee pre-specifies published or

Field	Content			
	other MIDs for specific outcomes • For risk ratios: 0.8 and 1.25. • For continuous outcomes: +/-0.5 times the baseline SD of the control arm. If there are 2 studies, the MID is calculated as +/- 0.5 times the mean of the SDs of the control arms at baseline. • Validity • The confidence in the findings across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group: http://www.gradeworkinggroup.org/			
Analysis of sub-groups (stratification)	None			
Type and method of review	☒	Intervention		
	☐	Diagnostic		
	☐	Prognostic		
	☐	Qualitative		
	☐	Epidemiologic		
	☐	Service Delivery		
	☐	Other (please specify)		
Language	English			
Country	England			
Anticipated or actual start date	6th Aug 2019			
Anticipated completion date	7th April 2021			
Stage of review at time of this submission	Review stage		Started	Completed
	Preliminary searches		☑	☑
	Piloting of the study selection process		☑	☑

Field	Content		
	Formal screening of search results against eligibility criteria	☑	☑
	Data extraction	☑	☑
	Risk of bias (quality) assessment	☑	☑
	Data analysis	☑	☑
Named contact	5a. Named contact National Guideline Alliance 5b. Named contact e-mail epilepsies@nice.org.uk 5c. Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and National Guideline Alliance		
Review team members	The National Guideline Alliance technical team		
Funding sources/sponsor	This systematic review is being completed by the National Guideline Alliance which receives funding from NICE.		
Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.		
Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10112		
URL for published protocol	https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019146620		
Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such		

Field	Content
	as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
Keywords	Epilepsy; Childhood; Centrotemporal spikes; Antiepileptic Drug
Details of existing review of same topic by same authors	Not applicable
Additional information	Not applicable
Details of final publication	www.nice.org.uk

ASM: antiseizure medication; CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; CSWS: contiuous spike-wave of slow-wave sleep; DARE: The Database of Abstracts of Reviews of Effects; EEG: electroencephalogram; ESES: electrical status epilepticus in sleep; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HR: hazard ratio; HTA: Health Technology Assessment; IQ: intelligence quotient; MID: minimal important difference; NICE: National Institute for Health and Care Excellence; RCT: Randomised Controlled Trial; RoB: Risk of Bias; ROBIS: risk of bias in systematic reviews; RR: risk ratio; SD: standard deviation; SeLECTS: Self-limited epilepsy with centrotemporal spikes

Table 10: Economic review protocol for 2026 update

Field	Content
Review title	Effectiveness of ASMs (anti-seizure medications) for self-limited epilepsy with centrotemporal spikes (SeLECTS)
Objective	The objective of this review is to determine which antiseizure medications (ASMs) improve outcomes in those with self-limited epilepsy with centrotemporal spikes.
Inclusion criteria	**Populations**: Children and young people with confirmed self-limited epilepsy with centrotemporal spikes Interventions: The following ASMs and their combinations will be considered: • Carbamazepine • Clobazam • Gabapentin

Field	Content
	• Lacosamide • Levetiracetam • Oxcarbazepine • Sodium Valproate • Sulthiame • Topiramate • Lamotrigine • Zonisamide **Relevant comparative economic study design:** cost–utility analysis, cost–effectiveness analysis, cost–consequences analysis, comparative cost analysis or decision analytic model-based on or within-trial economic analyses OECD countries (except USA) Healthcare and personal social services cost perspective Studies published from 2011 High-quality studies in line with the NICE reference case (recent UK NHS/PSS cost-utility analyses using the QALY as the measure of outcome) are the most applicable to NICE decision making. Not all studies meeting the inclusion criteria will therefore necessarily be used in decision-making - see Review strategy below for details.
Exclusion criteria	Conference posters or abstract only studies – these do not provide sufficient information for quality assessment. Studies published before 2011 Studies from non-OECD countries or the USA Non-comparative economic analyses including cost-of-illness studies. Letters, editorials or commentaries, study protocols or reviews of economic evaluations (recent reviews will be ordered and the bibliographies will be checked for relevant individual economic studies, which will then be ordered and checked for eligibility). Non-English language papers. Studies considering exclusively intervention costs, e.g. medicine acquisition costs, without considering wider healthcare costs associated with the management of epilepsy. Studies comparing costs of branded vs generic forms of the same medicine.

Field	Content
	Studies only focussing on productivity losses or gains.
Search strategy	The following bibliographic databases will be searched: Medline ALL (Ovid platform) Embase (Ovid platform) INAHTA International HTA Database The guideline committee or other stakeholders will be asked for details of any additional, relevant studies they may be aware of. The full search strategies for all databases will be published as an appendix to the final evidence review.
Review strategy	Studies meeting the inclusion and exclusion criteria will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist in appendix H of Developing NICE guidelines: the manual. The NICE economic evaluation checklist assesses: Applicability to the NICE guideline decision making context with consideration of the NICE reference case relevant to the guideline. Recent UK studies that use the NICE reference case methods are the most applicable when considering cost effectiveness. Methodological limitations. The aim is to present the best available economic evidence to inform committee decision-making in the context of the guideline, the current UK NHS setting and NICE methods. Therefore, the health economist may not present all studies that meet inclusion criteria. Studies that are deemed not applicable or have very serious methodological limitations should not inform committee decision-making. If recent high quality, UK cost-utility analyses are available for a question, it is often not deemed informative to present studies that are less applicable or lower quality such as older UK analyses or analyses from other countries. A similar principle is deemed to apply more generally when considering applicability and methodological limitations. Some specific examples are given below: If multiple versions of a model are available for the UK and other countries it is usually reasonable to only present the UK version. If multiple versions of the same UK model are available, it is usually reasonable to present only the most recent. If there has been a NICE MTA or guideline model that informs current NHS practice it is usually reasonable not to present older studies, unless they address a different subpopulation or other specific issue. If a UK model that includes all interventions in the decision space is available it may be reasonable not to present studies that only include individual or fewer interventions, if the analysis is sufficiently applicable and of good methodological quality. Quality and relevance of effectiveness data used in the economic analysis: the more closely the clinical effectiveness data used in the economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-

Field	Content
	making in the guideline. Hierarchy of economic evaluation evidence based on quality assessment 'Directly applicable' and 'Minor limitations' (only recent UK CUAs can get this rating). Usually presented and used in decision-making. Directly or partially applicable combined with minor or potentially serious limitations (other than 1). Discretion over whether these are presented and used in decision-making, depending on the availability of more relevant evidence. 'Not applicable' or 'Very serious limitations'. Typically not presented and not used in decision-making. The health economist will make a decision based on the relative applicability and quality of the available evidence for each question, in discussion with the guideline committee if required. All decisions will be transparently reported in the evidence report. Studies that are presented to the committee and used in decision-making when formulating recommendations will be included in the summary tables and will have an evidence extraction. Other studies may not be presented to the committee in detail but will be listed, with the reason for not being presented to the committee and thus not used in decision-making being provided. Committee members can review and query the decision not to present studies with the health economist and will be provided with full details of these studies where requested.

Appendix B – Literature search strategies

Background and development

Search design and peer review

A NICE Senior Information Specialist (SIS) conducted the literature searches. The MEDLINE strategies below were quality assured (QA) by another NICE SIS. All translated search strategies were peer reviewed to ensure their accuracy. Both procedures were adapted from the Peer Review of Electronic Search Strategies Guideline Statement (for further details see: McGowan J et al. PRESS 2015 Guideline Statement. *Journal of Clinical Epidemiology*, 75, 40-46).

The principal search strategies were developed in MEDLINE (Ovid interface) and adapted, as appropriate, for use in the other sources listed in the protocol, taking into account their size, search functionality and subject coverage.

This search report is based on the requirements of the PRISMA Statement for Reporting Literature Searches in Systematic Reviews (for further details see: Rethlefsen M et al. PRISMA-S. *Systematic Reviews*, 10(1), 39).

Review management

The search results were managed in EPPI-Reviewer v5. Duplicates were removed in EPPI-R5 using a two-step process. First, automated deduplication is performed using a high-value algorithm. Second, manual deduplication is used to assess "low-probability" matches. All decisions made for the review can be accessed via the deduplication history.

Prior work

- The search was based on the previous search conducted for the NICE guideline NG217 Epilepsies in children, young people and adults published April 2022. The previous searches were adapted for the purposes of this update.
- The updated search strategies were tested using the 2021 included papers to ensure the search continued to retrieve these studies.

Search limits and other restrictions

Formats

Limits were applied in adherence to standard NICE practice (as set out in the Identifying the evidence chapter of the manual) and the eligibility criteria listed in the review protocol to exclude:

- Animal studies
- Editorials, letters, news items and commentaries
- Conference abstracts and posters
- Registry entries for ongoing clinical trials or those that contain no results
- Theses and dissertations
- Papers not published in the English language.

The limit to remove animal studies in the searches was the standard NICE practice, which has been adapted from:

> Dickersin K, Scherer R & Lefebvre C. (1994) Systematic reviews: identifying relevant studies for systematic reviews. *BMJ*, 309 (6964), 1286.

Date limits

A date limit of 23 February 2021 to 10 December 2025 was applied, as stated in the review protocol, to find studies since the last searches were conducted for this guideline.

For the searches for economic evidence a date limit of 1 January 2011 to 27 February 2026 was applied as stated in the review protocol.

Search filters and classifiers

Cost effectiveness searches

In line with the review protocol, the sensitive version of the validated NICE cost utility filter was used in the MEDLINE and Embase strategies without amendment.

> Hubbard W et al. (2022) Development and validation of paired MEDLINE and Embase search filters for cost-utility studies. *BMC Medical Research Methodology*, 22(1), 310.

The following search filters were applied to the search strategies in MEDLINE and Embase to identify cost-effectiveness studies:

> Glanville J et al. (2009) Development and Testing of Search Filters to Identify Economic Evaluations in MEDLINE and EMBASE. Alberta: Canadian Agency for Drugs and Technologies in Health (CADTH)

> Arber, M et al. (2017) Performance of Ovid MEDLINE search filters to identify health state utility studies. International Journal of Health Technology Assessment in Health Care, 33(4), 472-480

Note: Several modifications have been made to these filters over the years that are standard NICE practice.

Key decisions

The search reused the same population parameters as the 2021 search and was updated from its original multifile format. Truncation and proximity operators were reviewed and applied consistently throughout. All proprietary and brand-name medications were cross-checked against the BNF and BNFc, with any names not included in the previous strategy added accordingly. The databases searched were consistent with those used in 2021.

1 Effectiveness searches

Database results

2

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	10/12/2025	Wiley	Issue 11 of 12, November 2025	1
Cochrane Database of Systematic Reviews (CDSR)	10/12/2025	Wiley	Issue 12 of 12, December 2025	5
Embase	10/12/2025	Ovid	1974 to 2025 December 08	77
Emcare	10/12/2025	Ovid	1995 to 2025 Week 48	10
Epistemonikos	10/12/2025	https://www.epistemonikos.org/	N/A	39
International HTA Database	10/12/2025	https://database.inahta.org/	N/A	0
MEDLINE ALL	10/12/2025	Ovid	1946 to December 09, 2025	57

3 Search strategy history

4 **Database name: MEDLINE ALL**

Searches
1 Epilepsy, Rolandic/ (749)
2 (bcects or bects or brec).tw. (507)
3 (benign* adj4 epilep*).tw. (1851)
4 (benign* adj4 child* adj4 (convuls* or epilep* or seizure* or spasm*)).tw. (892)
5 (benign* adj4 neonat* adj4 (convuls* or epilep* or seizure* or spasm*)).tw. (407)
6 (benign* adj4 p?ediatric* adj4 (convuls* or epilep* or seizure* or spasm*)).tw. (13)
7 ((convuls* or epilep*) adj4 (centrotemporal* adj4 spike*)).tw. (622)
8 CECTS.tw. (61)
9 ((centralopathic* or centrotemporal* or temporal-central) adj4 (convuls* or epilep* or seizure*)).tw. (658)
10 ((sylvian* or postrolandic* or roland*) adj4 (convuls* or epilep* or seizure* or spasm*)).tw. (732)
11 or/1-10 (2916)
12 Carbamazepine/ (12323)
13 (amizepin* or carbagen* or carbamazepin* or carbazepin* or curatil* or epitol* or finlepsin* or neurotol* or tegretol*).tw. (19929)

Searches
14 Clobazam/ (579)
15 (chlorepin* or clobazam* or clobazepam* or clorepin* or frisium* or noiafren* or onfi* or perizam* or urbadan* or urbanil* or urbanyl* or zacco*).tw. (1438)
16 Gabapentin/ (4782)
17 (apogabapentin* or convalis* or dineurin* or gabalept* or gabaliquid* or geriasan* or gabapentin* or gabatin* or gantin* or gralis* or kaptin* or keneil* or neurontin* or neurotonin* or novogabapentin* or nupentin*).tw. (9268)
18 Lacosamide/ (792)
19 (erlosamid* or harkoserid* or lacosamid* or vimpat*).tw. (1517)
20 Levetiracetam/ (3145)
21 (desitrend* or elepsia* or eltam* or etiracetam* or keppra* or kopodex* or levetiracetam* or matever* or spritam*).tw. (6076)
22 Oxcarbazepine/ (1175)
23 (apydan* or carbamazepin* or oxcarbazepin* or oxocarbazepin* or oxrat* or oxtellar* or timox* or trileptal* or trileptin*).tw. (19334)
24 Valproic Acid/ (14845)
25 (convulsofin* or delepsin* or depacon* or depaken* or depakin* or depakot* or depalept* or deprakin* or diplexil* or diprosin* or divalproex* or dyzantil* or epilim* or epival* or episenta* or epival* or ergenyl* or ergenyl* or everiden* or goilim* or hexaquin* or labazen* or leptilan* or micropakin* or mylproin* or orfil* or orfiril* or orlept* or petilin* or propymal* or stavzor* or valberg* or valcot* or valepil* or valeptol* or valerin* or valhel* or valoin* or valpakin* or valparin* or valporal* or valprax* or valpro* or valsup* or vupral*).tw. (23001)
26 (conadil* or contravul* or elisal* or ospolot* or riker* or sulphenytam* or sulthiam* or sultiam* or trolon*).tw. (412)
27 Topiramate/ (3225)
28 (epitomax* or topamax*or acomicil* or ecuram* or epiramat* or epitoram* or erravia* or etopro* or fagodol* or jadix* or lusitrax* or maritop* or oritop* or piralep* or pirantal* or pirepil* or qudexy* or ramas* or sincronil* or talopam* or tiramat* or topaben* or topamac* or topepsil* or topibrain* or topilek* or topimark* or topimax* or topiramat* or topirator* or topit* or toramat* or torlepta* or trokendi*).tw. (10326)
29 Lamotrigine/ (3686)
30 (crisomet* or labileno* or lamepil* or lamictal* or lamictin* or lamiktal* or lamodex* or lamogin* or lamotrigin* or lamotrix* or neurium*).tw. (6729)
31 Zonisamide/ (845)
32 (desizon* or excegran* or excemid* or zonegran* or zonisamid*).tw. (1650)
33 or/12-32 (69726)
34 11 and 33 (343)
35 animals/ not humans/ (5369823)
36 animals/ (7795338)
37 exp Animals, Laboratory/ (1018855)
38 exp Animal Experimentation/ (10811)
39 exp Models, Animal/ (700093)
40 exp Rodentia/ (3771470)
41 (rat or rats or mouse or mice or rodent*).ti. (1548446)
42 or/36-41 (7932860)
43 42 not humans/ (5498657)
44 34 not 43 (342)
45 letter/ (1319168)
46 editorial/ (743247)
47 news/ (233253)
48 exp historical article/ (418111)

Searches
49 Anecdotes as Topic/ (4748)
50 comment/ (1058665)
51 (letter or comment*).ti. (223211)
52 or/45-51 (3064155)
53 randomized controlled trial/ or random*.ti,ab. (1835249)
54 52 not 53 (3035796)
55 44 not 54 (333)
56 limit 55 to english (269)
57 limit 56 to ed=20210220-20251210 (38)
58 limit 56 to dt=20210220-20251210 (46)
59 57 or 58 (57)

1 **Database name: Embase**

Searches
1 exp benign childhood epilepsy/ (6316)
2 (bcects or bects or brec).tw. (775)
3 (benign* adj4 epilep*).tw. (2860)
4 (benign* adj4 child* adj4 (convuls* or epilep* or seizure* or spasm*)).tw. (1319)
5 (benign* adj4 neonat* adj4 (convuls* or epilep* or seizure* or spasm*)).tw. (586)
6 (benign* adj4 p?ediatric* adj4 (convuls* or epilep* or seizure* or spasm*)).tw. (16)
7 ((convuls* or epilep*) adj4 (centrotemporal* adj4 spike*)).tw. (857)
8 CECTS.tw. (101)
9 ((centralopathic* or centrotemporal* or temporal-central) adj4 focal* adj4 (convuls* or epilep* or seizure*)).tw. (29)
10 ((sylvian* or postrolandic* or roland*) adj4 (convuls* or epilep* or seizure* or spasm*)).tw. (1153)
11 or/1-10 (9150)
12 *Carbamazepine/ (18410)
13 (amizepin* or carbamazepin* or carbazepin* or curatil* or epitol* or finlepsin* or neurotol* or tegretol*).tw,tn. (31599)
14 *Clobazam/ (1639)
15 (chlorepin* or clobazam* or clobazepam* or clorepin* or frisium* or noiafren* or onfi* or perizam* or urbadan* or urbanil* or urbanyl* or zacco*).tw,tn. (3191)
16 *Gabapentin/ (6088)
17 (apogabapentin* or convalis* or dineurin* or gabalept* or gabaliquid* or geriasan* or gabapentin* or gabatin* or gantin* or gralis* or kaptin* or keneil* or neurontin* or neurotonin* or novogabapentin* or nupentin*).tw,tn. (17975)
18 *Lacosamide/ (1770)
19 (erlosamid* or harkoserid* or lacosamid* or vimpat*).tw,tn. (3319)
20 *Levetiracetam/ (2421)
21 (desitrend* or elepsia* or eltam* or keppra* or kopodex* or levetiracetam* or matever* or spritam*).tw,tn. (13306)
22 *Oxcarbazepine/ (1773)
23 (apydan* or carbamazepin* or oxcarbazepin* or oxocarbazepin* or oxrat* or oxtellar* or timox* or trileptal* or trileptin*).tw,tn. (28421)
24 *Valproic Acid/ (20430)
25 (convulsofin* or delepsin* or depacon* or depaken* or depakin* or depakot* or depalept* or deprakin* or diplexil* or diprosin* or divalproex* or dyzantil* or epilim* or epival* or episenta* or epival* or ergenyl* or ergenyl* or everiden* or goilim* or hexaquin* or laba-

Searches
zen* or leptilan* or leptilanil* or micropakin* or mylproin* or orfil* or orfiril* or orlept* or petilin* or propymal* or stavzor* or valberg* or valcot* or valepil* or valeptol* or valerin* or valhel* or valoin* or valpakin* or valparin* or valporal* or valprax* or valpro* or valproate* or valprodura* or valprosid* or valprotek* or valsup* or vupral*).tw,tn. (38376)
26 *Sultiame/ (519)
27 (conadil* or contravul* or elisal* or ospolot* or riker* or sulphenytam* or sulthiam* or sultiam* or trolon*).tw,tn. (937)
28 *Topiramate/ (4401)
29 (epitomax* or topamax*or acomicil* or ecuram* or epiramat* or epitoram* or erravia* or etopro* or fagodol* or jadix* or lusitrax* or maritop* or oritop* or piralep* or pirantal* or pirepil* or qudexy* or ramas* or sincronil* or talopam* or tiramat* or topaben* or topamac* or topepsil* or topibrain* or topilek* or topimark* or topimax* or topiramat* or topirator* or topit* or toramat* or torlepta* or trokendi*).tw,tn. (14981)
30 *Lamotrigine/ (4936)
31 (crisomet* or labileno* or lamepil* or lamictal* or lamictin* or lamiktal* or lamodex* or lamogin* or lamotrigin* or lamotrix* or neurium*).tw,tn. (12200)
32 *Zonisamide/ (1339)
33 (desizon* or excegran* or excemid* or zonegran* or zonisamid*).tw,tn. (2900)
34 or/12-33 (116445)
35 11 and 34 (1249)
36 animal/ (1743119)
37 nonhuman/ (8416763)
38 exp Animal Experiment/ (3470774)
39 exp Experimental Animal/ (924988)
40 animal model/ (1999861)
41 exp Rodent/ (4430605)
42 (rat or rats or mouse or mice or rodent*).ti. (1745916)
43 or/36-42 (11055760)
44 43 not human/ (7785541)
45 35 not 44 (1243)
46 limit 45 to english language (1008)
47 conference*.db,pt,su. (6543414)
48 46 not 47 (754)
49 clinical trial.pt. (552954)
50 48 not 49 (747)
51 letter.pt. or letter/ (1411184)
52 note.pt. (1029218)
53 editorial.pt. (854970)
54 (letter or comment*).ti. (267930)
55 or/51-54 (3359858)
56 randomized controlled trial/ or random*.ti,ab. (2686706)
57 55 not 56 (3321456)
58 50 not 57 (717)
59 limit 58 to dc=20210223-20251210 (77)
60 limit 58 to dd=20210223-20251210 (68)
61 59 or 60 (77)

1 **Database name: Cochrane Library**

Searches
#1 MeSH descriptor: [Epilepsy, Rolandic] this term only 24
#2 ((bcects or bects or brec).tw):ti,ab,kw 586
#3 ((benign* near/4 epilep*)):ti,ab,kw 136
#4 (((benign* near/4 child*) near/4 (convuls* or epilep* or seizure* or spasm*))):ti,ab,kw 108
#5 (((benign* near/4 neonat*) near/4 (convuls* or epilep* or seizure* or spasm*))):ti,ab,kw 7
#6 (((benign* near/4 p?ediatric*) near/4 (convuls* or epilep* or seizure* or spasm*))):ti,ab,kw 1
#7 (((convuls* or epilep*) near/4 (centrotemporal* near/4 spike*))):ti,ab,kw 38
#8 (CECTS):ti,ab,kw 4
#9 (((centralopathic* or centrotemporal* or temporal-central) near/4 (convuls* or epilep* or seizure*))):ti,ab,kw 39
#10 (((sylvian* or postrolandic* or roland*) near/4 (convuls* or epilep* or seizure* or spasm*))):ti,ab,kw 56
#11 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 754
#12 MeSH descriptor: [Carbamazepine] this term only 960
#13 ((amizepin* or carbagen* or carbamazepin* or carbazepin* or curatil* or epitol* or finlepsin* or neurotol* or tegretol*)):ti,ab,kw 2299
#14 MeSH descriptor: [Clobazam] this term only 101
#15 ((chlorepin* or clobazam* or clobazepam* or clorepin* or frisium* or noiafren* or onfi* or perizam* or urbadan* or urbanil* or urbanyl* or zacco*)):ti,ab,kw 442
#16 MeSH descriptor: [Gabapentin] this term only 1084
#17 ((apogabapentin* or convalis* or dineurin* or gabalept* or gabaliquid* or geriasan* or gabapentin* or gabatin* or gantin* or gralis* or kaptin* or keneil* or neurontin* or neurotonin* or novogabapentin* or nupentin*)):ti,ab,kw 3269
#18 MeSH descriptor: [Lacosamide] this term only 139
#19 ((erlosamid* or harkoserid* or lacosamid* or vimpat*)):ti,ab,kw 356
#20 MeSH descriptor: [Levetiracetam] this term only 467
#21 ((desitrend* or elepsia* or eltam* or etiracetam* or keppra* or kopodex* or levetiracetam* or matever* or spritam*)):ti,ab,kw 1267
#22 MeSH descriptor: [Oxcarbazepine] this term only 168
#23 ((apydan* or carbamazepin* or oxcarbazepin* or oxocarbazepin* or oxrat* or oxtellar* or timox* or trileptal* or trileptin*)):ti,ab,kw 2433
#24 MeSH descriptor: [Valproic Acid] this term only 1160
#25 ((convulsofin* or delepsin* or depacon* or depaken* or depakin* or depakot* or depalept* or deprakin* or diplexil* or diprosin* or divalproex* or dyzantil* or epilim* or epival* or episenta* or epival* or ergenyl* or ergenyl* or everiden* or goilim* or hexaquin* or labazen* or leptilan* or micropakin* or mylproin* or orfil* or orfiril* or orlept* or petilin* or propymal* or stavzor* or valberg* or valcot* or valepil* or valeptol* or valerin* or valhel* or valoin* or valpakin* or valparin* or valporal* or valprax* or valpro* or valsup* or vupral*)):ti,ab,kw 3118
#26 ((conadil* or contravul* or elisal* or ospolot* or riker* or sulphenytam* or sulthiam* or sultiam* or trolon*)):ti,ab,kw 238
#27 MeSH descriptor: [Topiramate] this term only 696
#28 ((epitomax* or topamax*or acomicil* or ecuram* or epiramat* or epitoram* or erravia* or etopro* or fagodol* or jadix* or lusitrax* or maritop* or oritop* or piralep* or pirantal* or pirepil* or qudexy* or ramas* or sincronil* or talopam* or tiramat* or topaben* or topamac* or topepsil* or topibrain* or topilek* or topimark* or topimax* or topiramat* or topirator* or topit* or toramat* or torlepta* or trokendi*)):ti,ab,kw 1766
#29 MeSH descriptor: [Lamotrigine] this term only 536
#30 ((crisomet* or labileno* or lamepil* or lamictal* or lamictin* or lamiktal* or lamodex* or lamogin* or lamotrigin* or lamotrix* or neurium*)):ti,ab,kw 1356

Searches
#31 MeSH descriptor: [Zonisamide] this term only 139
#32 ((desizon* or excegran* or excemid* or zonegran* or zonisamid*)):ti,ab,kw 363
#33 {or #12-#32} 11934
#34 #11 and #33 73
#35 "conference":pt or (clinicaltrials or trialsearch):so 871674
#36 #34 not #35 with Cochrane Library publication date Between Feb 2021 and Dec 2025 6

1 **Database name: Emcare**

Searches
1 exp benign childhood epilepsy/ (1210)
2 (bcects or bects or brec).tw. (78)
3 (benign* adj4 epilep*).tw. (259)
4 (benign* adj4 child* adj4 (convuls* or epilep* or seizure* or spasm*)).tw. (122)
5 (benign* adj4 neonat* adj4 (convuls* or epilep* or seizure* or spasm*)).tw. (63)
6 (benign* adj4 p?ediatric* adj4 (convuls* or epilep* or seizure* or spasm*)).tw. (1)
7 ((convuls* or epilep*) adj4 (centrotemporal* adj4 spike*)).tw. (94)
8 CECTS.tw. (30)
9 ((centralopathic* or centrotemporal* or temporal-central) adj4 focal* adj4 (convuls* or epilep* or seizure*)).tw. (1)
10 ((sylvian* or postrolandic* or roland*) adj4 (convuls* or epilep* or seizure* or spasm*)).tw. (121)
11 or/1-10 (1495)
12 *Carbamazepine/ (1184)
13 (amizepin* or carbamazepin* or carbazepin* or curatil* or epitol* or finlepsin* or neurotol* or tegretol*).tw,tn. (3512)
14 *Clobazam/ (69)
15 (chlorepin* or clobazam* or clobazepam* or clorepin* or frisium* or noiafren* or onfi* or perizam* or urbadan* or urbanil* or urbanyl* or zacco*).tw,tn. (256)
16 *Gabapentin/ (1831)
17 (apogabapentin* or convalis* or dineurin* or gabalept* or gabaliquid* or geriasan* or gabapentin* or gabatin* or gantin* or gralis* or kaptin* or keneil* or neurontin* or neurotonin* or novogabapentin* or nupentin*).tw,tn. (4343)
18 *Lacosamide/ (105)
19 (erlosamid* or harkoserid* or lacosamid* or vimpat*).tw,tn. (335)
20 *Levetiracetam/ (389)
21 (desitrend* or elepsia* or eltam* or keppra* or kopodex* or levetiracetam* or matever* or spritam*).tw,tn. (1547)
22 *Oxcarbazepine/ (246)
23 (apydan* or carbamazepin* or oxcarbazepin* or oxocarbazepin* or oxrat* or oxtellar* or timox* or trileptal* or trileptin*).tw,tn. (2821)
24 *Valproic Acid/ (2052)
25 (convulsofin* or delepsin* or depacon* or depaken* or depakin* or depakot* or depalept* or deprakin* or diplexil* or diprosin* or divalproex* or dyzantil* or epilim* or epival* or episenta* or epival* or ergenyl* or ergenyl* or everiden* or goilim* or hexaquin* or labazen* or leptilan* or leptilanil* or micropakin* or mylproin* or orfil* or orfiril* or orlept* or petilin* or propymal* or stavzor* or valberg* or valcot* or valepil* or valeptol* or valerin* or valhel* or valoin* or valpakin* or valparin* or valporal* or valprax* or valpro* or valproate* or valprodura* or valprosid* or valprotek* or valsup* or vupral*).tw,tn. (4811)
26 *Sultiame/ (24)

Searches
27 (conadil* or contravul* or elisal* or ospolot* or riker* or sulphenytam* or sulthiam* or sultiam* or trolon*).tw,tn. (119)
28 *Topiramate/ (910)
29 (epitomax* or topamax*or acomicil* or ecuram* or epiramat* or epitoram* or erravia* or etopro* or fagodol* or jadix* or lusitrax* or maritop* or oritop* or piralep* or pirantal* or pirepil* or qudexy* or ramas* or sincronil* or talopam* or tiramat* or topaben* or topamac* or topepsil* or topibrain* or topilek* or topimark* or topimax* or topiramat* or topirator* or topit* or toramat* or torlepta* or trokendi*).tw,tn. (1766)
30 *Lamotrigine/ (831)
31 (crisomet* or labileno* or lamepil* or lamictal* or lamictin* or lamiktal* or lamodex* or lamogin* or lamotrigin* or lamotrix* or neurium*).tw,tn. (1861)
32 *Zonisamide/ (169)
33 (desizon* or excegran* or excemid* or zonegran* or zonisamid*).tw,tn. (409)
34 or/12-33 (15498)
35 11 and 34 (114)
36 animal/ (13630)
37 nonhuman/ (1044071)
38 exp Animal Experiment/ (403773)
39 exp Experimental Animal/ (95090)
40 animal model/ (294639)
41 exp Rodent/ (400971)
42 (rat or rats or mouse or mice or rodent*).ti. (163444)
43 or/36-42 (1110160)
44 43 not human/ (645081)
45 35 not 44 (113)
46 limit 45 to english language (106)
47 conference*.db,pt,su. (184264)
48 46 not 47 (104)
49 clinical trial.pt. (0)
50 48 not 49 (104)
51 letter.pt. or letter/ (459337)
52 note.pt. (400073)
53 editorial.pt. (367583)
54 (letter or comment*).ti. (85404)
55 or/51-54 (1239273)
56 randomized controlled trial/ or random*.ti,ab. (752141)
57 55 not 56 (1223520)
58 50 not 57 (97)
59 limit 58 to dc=20210223-20251210 (10)
60 limit 58 to dd=20210223-20251210 (6)
61 59 or 60 (10)

1 **Database name: Epistemonikos**

Searches
1 (title:((bcects OR bects OR brec)) OR abstract:((bcects OR bects OR brec)))
2 (title:((benign* AND epilep*)) OR abstract:((benign* AND epilep*)))
3 (title:(benign*) OR abstract:(benign*)) AND (title:(child*) OR abstract:(child*)) AND (title:((convuls* OR epilep* OR seizure* OR spasm*)) OR abstract:((convuls* OR epilep* OR

Searches
seizure* OR spasm*)))
4 (title:(benign*) OR abstract:(benign*)) AND (title:(neonat*) OR abstract:(neonat*)) AND (title:((convuls* OR epilep* OR seizure* OR spasm*)) OR abstract:((convuls* OR epilep* OR seizure* OR spasm*)))
5 (title:(benign*) OR abstract:(benign*)) AND (title:(paediatric*) OR abstract:(paediatric*)) AND (title:((convuls* OR epilep* OR seizure* OR spasm*)) OR abstract:((convuls* OR epilep* OR seizure* OR spasm*)))
6 (title:(benign*) OR abstract:(benign*)) AND (title:(pediatric*) OR abstract:(pediatric*)) AND (title:((convuls* OR epilep* OR seizure* OR spasm*)) OR abstract:((convuls* OR epilep* OR seizure* OR spasm*)))
7 (title:((convuls* OR epilep*)) OR abstract:((convuls* OR epilep*))) AND (title:((centrotemporal* AND spike*)) OR abstract:((centrotemporal* AND spike*)))
8 (title:(CECTS) OR abstract:(CECTS))
9 (title:((centralopathic* OR centrotemporal* OR temporal-central)) OR abstract:((centralopathic* OR centrotemporal* OR temporal-central))) AND (title:((convuls* OR epilep* OR seizure*)) OR abstract:((convuls* OR epilep* OR seizure*)))
10 (title:((sylvian* OR postrolandic* OR roland*)) OR abstract:((sylvian* OR postrolandic* OR roland*))) AND (title:((convuls* OR epilep* OR seizure* OR spasm*)) OR abstract:((convuls* OR epilep* OR seizure* OR spasm*)))

1 **Database name: INAHTA**

Searches
1 "Epilepsy, Rolandic"[mh] (0)
2 ((bcects or bects or brec))[Title] OR ((bcects or bects or brec))[abs] (0)
3 ((benign* AND epilep*))[Title] OR ((benign* AND epilep*)) (1)
4 (((benign AND child*) AND (convuls* or epilep* or seizure* or spasm*)))[Title] OR (((benign AND child*) AND (convuls* or epilep* or seizure* or spasm*)))[abs] (1)
5 (((benign AND neonat*) AND (convuls* or epilep* or seizure* or spasm*)))[Title] OR (((benign AND neonat*) AND (convuls* or epilep* or seizure* or spasm*)))[abs] (0)
6 (((benign AND paediatric*) AND (convuls* or epilep* or seizure* or spasm*)))[Title] OR (((benign AND paediatric*) AND (convuls* or epilep* or seizure* or spasm*)))[abs] (0)
7 (((benign AND pediatric*) AND (convuls* or epilep* or seizure* or spasm*)))[Title] OR (((benign AND pediatric*) AND (convuls* or epilep* or seizure* or spasm*)))[abs] (0)
8 (((convuls* or epilep*) AND (centrotemporal* AND spike*)))[Title] OR (((convuls* or epilep*) AND (centrotemporal* AND spike*)))[abs] (1)
9 (CECTS)[Title] OR (CECTS)[abs] (0)
10 (((centralopathic* or centrotemporal* or temporal-central) AND (convuls* or epilep* or seizure*)))[Title] OR (((centralopathic* or centrotemporal* or temporal-central) AND (convuls* or epilep* or seizure*)))[abs] (1)
11 (((sylvian* or postrolandic* or roland*) AND (convuls* or epilep* or seizure* or spasm*)))[Title] OR (((sylvian* or postrolandic* or roland*) AND (convuls* or epilep* or seizure* or spasm*)))[abs] (0)
12 #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1 (1) (Date limited to 2011 – 2026 (0)

2

1 Cost-effectiveness searches

Database results

2

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Embase	27/02/2026	Ovid	1974 to 2026 February 25	11
International HTA Database	27/02/2026	https://database.inahta.org/	-	0
MEDLINE	27/02/2026	Ovid	1946 to February 26, 2026	3

3 Search strategy history

4 **Database name: MEDLINE ALL**

Searches
Ovid MEDLINE(R) ALL <1946 to February 26, 2026> 1 Epilepsy, Rolandic/ 757 2 (bcects or bects or brec).tw. 507 3 (benign* adj4 epilep*).tw. 1857 4 (benign adj4 child* adj4 (convuls* or epilep* or seizure* or spasm*)).tw. 893 5 (benign adj4 neonat* adj4 (convuls* or epilep* or seizure* or spasm*)).tw. 407 6 (benign adj4 p?ediatric* adj4 (convuls* or epilep* or seizure* or spasm*)).tw. 13 7 ((convuls* or epilep*) adj4 (centrotemporal* adj4 spike*)).tw. 631 8 CECTS.tw. 61 9 ((centralopathic* or centrotemporal* or temporal-central) adj4 (convuls* or epilep* or seizure*)).tw. 667 10 ((sylvian* or postrolandic* or roland*) adj4 (convuls* or epilep* or seizure* or spasm*)).tw. 732 11 or/1-10 2930 12 Carbamazepine/ 12349 13 (amizepin* or carbagen* or carbamazepin* or carbazepin* or curatil* or epitol* or finlepsin* or neurotol* or tegretol*).tw. 20040 14 Clobazam/ 582 15 (chlorepin* or clobazam* or clobazepam* or clorepin* or frisium* or noiafren* or onfi* or perizam* or urbadan* or urbanil* or urbanyl* or zacco*).tw. 1456 16 Gabapentin/ 4809 17 (apogabapentin* or convalis* or dineurin* or gabalept* or gabaliquid* or geriasan* or gabapentin* or gabatin* or gantin* or gralis* or kaptin* or keneil* or neurontin* or neurotonin* or novogabapentin* or nupentin*).tw. 9398 18 Lacosamide/ 801 19 (erlosamid* or harkoserid* or lacosamid* or vimpat*).tw. 1544 20 Levetiracetam/ 3173 21 (desitrend* or elepsia* or eltam* or etiracetam* or keppra* or kopodex* or levetiracetam* or matever* or spritam*).tw. 6186 22 Oxcarbazepine/ 1181

Searches
23 (apydan* or carbamazepin* or oxcarbazepin* or oxocarbazepin* or oxrat* or oxtellar* or timox* or trileptal* or trileptin*).tw. 19446
24 Valproic Acid/ 14905
25 (convulsofin* or delepsin* or depacon* or depaken* or depakin* or depakot* or depalept* or deprakin* or diplexil* or diprosin* or divalproex* or dyzantil* or epilim* or epival* or episenta* or epival* or ergenyl* or ergenyl* or everiden* or goilim* or hexaquin* or labazen* or leptilan* or micropakin* or mylproin* or orfil* or orfiril* or orlept* or petilin* or propymal* or stavzor* or valberg* or valcot* or valepil* or valeptol* or valerin* or valhel* or valoin* or valpakin* or valparin* or valporal* or valprax* or valpro* or valsup* or vupral*).tw. 23187
26 (conadil* or contravul* or elisal* or ospolot* or riker* or sulphenytam* or sulthiam* or sultiam* or trolon*).tw. 413
27 Topiramate/ 3241
28 (epitomax* or topamax*or acomicil* or ecuram* or epiramat* or epitoram* or erravia* or etopro* or fagodol* or jadix* or lusitrax* or maritop* or oritop* or piralep* or pirantal* or pirepil* or qudexy* or ramas* or sincronil* or talopam* or tiramat* or topaben* or topamac* or topepsil* or topibrain* or topilek* or topimark* or topimax* or topiramat* or topirator* or topit* or toramat* or torlepta* or trokendi*).tw. 10382
29 Lamotrigine/ 3702
30 (crisomet* or labileno* or lamepil* or lamictal* or lamictin* or lamiktal* or lamodex* or lamogin* or lamotrigin* or lamotrix* or neurium*).tw. 6791
31 Zonisamide/ 847
32 (desizon* or excegran* or excemid* or zonegran* or zonisamid*).tw. 1663
33 or/12-32 70306
34 11 and 33 345
35 animals/ not humans/ 5392823
36 animals/ 7843315
37 exp Animals, Laboratory/ 1027073
38 exp Animal Experimentation/ 10840
39 exp Models, Animal/ 706978
40 exp Rodentia/ 3793899
41 (rat or rats or mouse or mice or rodent*).ti. 1555457
42 or/36-41 7982977
43 42 not humans/ 5523776
44 34 not 43 344
45 letter/ 1328682
46 editorial/ 750023
47 news/ 234376
48 exp historical article/ 418900
49 Anecdotes as Topic/ 4748
50 comment/ 1061075
51 (letter or comment*).ti. 226968
52 or/45-51 3084565
53 randomized controlled trial/ or random*.ti,ab. 1859704
54 52 not 53 3056232
55 44 not 54 335
56 limit 55 to english 271
57 limit 56 to ed=20110101-20260227 115
58 limit 56 to dt=20110101-20260227 140
59 57 or 58 143

Searches
60 Cost-Benefit Analysis/ 100395
61 Quality-Adjusted Life Years/ 18980
62 Markov Chains/ 17850
63 exp Models, Economic/ 17199
64 cost*.ti. 163990
65 (cost* adj2 utilit*).tw. 9269
66 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw. 346035
67 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. 58239
68 (qualit* adj2 adjust* adj2 life*).tw. 21570
69 QALY*.tw. 17605
70 (incremental* adj2 cost*).tw. 20965
71 ICER.tw. 7838
72 utilities.tw. 10974
73 markov*.tw. 37755
74 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. 61927
75 ((utility or effective*) adj2 analys*).tw. 30686
76 (willing* adj2 pay*).tw. 12554
77 (EQ5D* or EQ-5D*).tw. 17559
78 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. 5318
79 (european* adj2 quality adj3 ("5" or five)).tw. 932
80 or/60-79 602692
81 Quality-Adjusted Life Years/ 18980
82 (quality adjusted or adjusted life year$).ti,ab,kf. 32077
83 (qaly$ or qald$ or qale$ or qtime$).ti,ab,kf. 18108
84 (illness state$1 or health state$1).ti,ab,kf. 9843
85 (hui or hui1 or hui2 or hui3).ti,ab,kf. 2334
86 (multiattribute$ or multi attribute$).ti,ab,kf. 1724
87 (utility adj3 (score$1 or valu$ or health$ or cost$ or measur$ or disease$ or mean or gain or gains or index$)).ti,ab,kf. 25145
88 utilities.ti,ab,kf. 11112
89 (eq-5d or eq5d or eq-5 or eq5 or euro qual or euroqual or euro qual5d or euroqual5d or euro qol or euroqol or euro qol5d or euroqol5d or euro quol or euroquol or euro quol5d or euroquol5d or eur qol or euroqol or eur qol5d or eur?qul or eur?qul5d or euro$ quality of life or european qol).ti,ab,kf. 22845
90 (euro$ adj3 (5 d or 5d or 5 dimension$ or 5dimension$ or 5 domain$ or 5domain$)).ti,ab,kf. 7728
91 (sf36$ or sf 36$ or sf thirtysix or sf thirty six).ti,ab,kf. 30472
92 (time trade off$1 or time tradeoff$1 or tto or timetradeoff$1).ti,ab,kf. 2898
93 quality of life/ and ((quality of life or qol) adj (score$1 or measure$1)).ti,ab,kf. 18840
94 quality of life/ and ec.fs. 11778
95 quality of life/ and (health adj3 status).ti,ab,kf. 13609
96 (quality of life or qol).ti,ab,kf. and Cost-Benefit Analysis/ 19935
97 ((qol or hrqol or quality of life).ti,kf. or *quality of life/) and ((qol or hrqol$ or quality of life) adj2 (increas$ or decrease$ or improv$ or declin$ or reduc$ or high$ or low$ or effect or effects or worse or score or scores or change$1 or impact$1 or impacted or deterio-

Searches
rat$)).ab. 68779
98 Cost-Benefit Analysis/ and (cost-effectiveness ratio$ and (perspective$ or life expectanc$)).ti,ab,kf. 6454
99 *quality of life/ and (quality of life or qol).ti. 74368
100 quality of life/ and ((quality of life or qol) adj3 (improv$ or chang$)).ti,ab,kf. 51619
101 quality of life/ and health-related quality of life.ti,ab,kf. 53829
102 models, economic/ 11936
103 or/81-102 271698
104 Economics/ 27558
105 Value of life/ 5854
106 exp "Costs and Cost Analysis"/ 285946
107 exp Economics, Hospital/ 26442
108 exp Economics, Medical/ 14481
109 Economics, Nursing/ 4015
110 Economics, Pharmaceutical/ 3178
111 exp "Fees and Charges"/ 31845
112 exp Budgets/ 14466
113 budget*.ti,ab. 41570
114 cost*.ti. 163990
115 (economic* or pharmaco?economic*).ti. 70967
116 (price* or pricing*).ti,ab. 63184
117 (cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab. 265751
118 (financ* or fee or fees).ti,ab. 197517
119 (value adj2 (money or monetary)).ti,ab. 3598
120 or/104-119 861082
121 59 and 80 2
122 59 and 103 1
123 59 and 120 1
124 121 or 122 or 123 3

1 **Database name: Embase**

Searches
Database: Embase <1974 to 2026 February 24>
Search Strategy:
---
1 exp benign childhood epilepsy/ (6338)
2 (bcects or bects or brec).tw. (780)
3 (benign* adj4 epilep*).tw. (2878)
4 (benign adj4 child* adj4 (convuls* or epilep* or seizure* or spasm*)).tw. (1322)
5 (benign adj4 neonat* adj4 (convuls* or epilep* or seizure* or spasm*)).tw. (587)
6 (benign adj4 p?ediatric* adj4 (convuls* or epilep* or seizure* or spasm*)).tw. (16)
7 ((convuls* or epilep*) adj4 (centrotemporal* adj4 spike*)).tw. (878)
8 CECTS.tw. (102)
9 ((centralopathic* or centrotemporal* or temporal-central) adj4 focal* adj4 (convuls* or

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epilep* or seizure*)).tw. (30)
10 ((sylvian* or postrolandic* or roland*) adj4 (convuls* or epilep* or seizure* or spasm*)).tw. (1157)
11 or/1-10 (9194)
12 *Carbamazepine/ (18469)
13 (amizepin* or carbamazepin* or carbazepin* or curatil* or epitol* or finlepsin* or neurotol* or tegretol*).tw,tn. (31897)
14 *Clobazam/ (1649)
15 (chlorepin* or clobazam* or clobazepam* or clorepin* or frisium* or noiafren* or onfi* or perizam* or urbadan* or urbanil* or urbanyl* or zacco*).tw,tn. (3289)
16 *Gabapentin/ (6164)
17 (apogabapentin* or convalis* or dineurin* or gabalept* or gabaliquid* or geriasan* or gabapentin* or gabatin* or gantin* or gralis* or kaptin* or keneil* or neurontin* or neurotonin* or novogabapentin* or nupentin*).tw,tn. (18389)
18 *Lacosamide/ (1797)
19 (erlosamid* or harkoserid* or lacosamid* or vimpat*).tw,tn. (3439)
20 *Levetiracetam/ (2489)
21 (desitrend* or elepsia* or eltam* or keppra* or kopodex* or levetiracetam* or matever* or spritam*).tw,tn. (13758)
22 *Oxcarbazepine/ (1779)
23 (apydan* or carbamazepin* or oxcarbazepin* or oxocarbazepin* or oxrat* or oxtellar* or timox* or trileptal* or trileptin*).tw,tn. (28730)
24 *Valproic Acid/ (20549)
25 (convulsofin* or delepsin* or depacon* or depaken* or depakin* or depakot* or depalept* or deprakin* or diplexil* or diprosin* or divalproex* or dyzantil* or epilim* or epival* or episenta* or epival* or ergenyl* or ergenyl* or everiden* or goilim* or hexaquin* or labazen* or leptilan* or leptilanil* or micropakin* or mylproin* or orfil* or orfiril* or orlept* or petilin* or propymal* or stavzor* or valberg* or valcot* or valepil* or valeptol* or valerin* or valhel* or valoin* or valpakin* or valparin* or valporal* or valprax* or valpro* or valproate* or valprodura* or valprosid* or valprotek* or valsup* or vupral*).tw,tn. (38903)
26 *Sultiame/ (519)
27 (conadil* or contravul* or elisal* or ospolot* or riker* or sulphenytam* or sulthiam* or sultiam* or trolon*).tw,tn. (943)
28 *Topiramate/ (4424)
29 (epitomax* or topamax*or acomicil* or ecuram* or epiramat* or epitoram* or erravia* or etopro* or fagodol* or jadix* or lusitrax* or maritop* or oritop* or piralep* or pirantal* or pirepil* or qudexy* or ramas* or sincronil* or talopam* or tiramat* or topaben* or topamac* or topepsil* or topibrain* or topilek* or topimark* or topimax* or topiramat* or topirator* or topit* or toramat* or torlepta* or trokendi*).tw,tn. (15163)
30 *Lamotrigine/ (4977)
31 (crisomet* or labileno* or lamepil* or lamictal* or lamictin* or lamiktal* or lamodex* or lamogin* or lamotrigin* or lamotrix* or neurium*).tw,tn. (12400)
32 *Zonisamide/ (1346)
33 (desizon* or excegran* or excemid* or zonegran* or zonisamid*).tw,tn. (2935)
34 or/12-33 (118161)
35 11 and 34 (1253)
36 animal/ (1752830)
37 nonhuman/ (8528375)
38 exp Animal Experiment/ (3518461)
39 exp Experimental Animal/ (939418)
40 animal model/ (2034180)

Searches
41 exp Rodent/ (4477187)
42 (rat or rats or mouse or mice or rodent*).ti. (1757307)
43 or/36-42 (11180204)
44 43 not human/ (7857609)
45 35 not 44 (1247)
46 limit 45 to english language (1011)
47 conference*.db,pt,su. (6728568)
48 46 not 47 (756)
49 clinical trial.pt. (552952)
50 48 not 49 (749)
51 letter.pt. or letter/ (1423916)
52 note.pt. (1037215)
53 editorial.pt. (862995)
54 (letter or comment*).ti. (271408)
55 or/51-54 (3389032)
56 randomized controlled trial/ or random*.ti,ab. (2736616)
57 55 not 56 (3350151)
58 50 not 57 (719)
59 limit 58 to dc=20110101-20260227 (351)
60 limit 58 to dd=20110101-20260227 (351)
61 59 or 60 (351)
62 cost utility analysis/ (14979)
63 quality adjusted life year/ (43702)
64 cost*.ti. (222021)
65 (cost* adj2 utilit*).tw. (15559)
66 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw. (485215)
67 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. (83202)
68 (qualit* adj2 adjust* adj2 life*).tw. (33252)
69 QALY*.tw. (32664)
70 (incremental* adj2 cost*).tw. (34624)
71 ICER.tw. (16386)
72 utilities.tw. (17668)
73 markov*.tw. (47716)
74 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. (86492)
75 ((utility or effective*) adj2 analys*).tw. (46986)
76 (willing* adj2 pay*).tw. (18571)
77 (EQ5D* or EQ-5D*).tw. (35264)
78 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. (7273)
79 (european* adj2 quality adj3 ("5" or five)).tw. (1353)
80 or/62-79 (780985)
81 Health economics/ (38111)
82 exp health care cost/ (386084)
83 exp Fee/ (48101)
84 exp Budget/ (38521)

Searches
85 Funding/ (84225)
86 budget*.ti,ab. (55863)
87 cost*.ti. (222021)
88 (economic* or pharmaco?economic*).ti. (89382)
89 (price* or pricing*).ti,ab. (86924)
90 (cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab. (369707)
91 (financ* or fee or fees).ti,ab. (292173)
92 (value adj2 (money or monetary)).ti,ab. (4823)
93 or/81-92 (1270764)
94 Quality-Adjusted Life Year/ (43702)
95 (quality adjusted or adjusted life year$).ti,ab,kf. (46545)
96 (qaly$ or qald$ or qale$ or qtime$).ti,ab,kf. (33444)
97 (illness state$1 or health state$1).ti,ab,kf. (17487)
98 (hui or hui1 or hui2 or hui3).ti,ab,kf. (3975)
99 (multiattribute$ or multi attribute$).ti,ab,kf. (1959)
100 (utility adj3 (score$1 or valu$ or health$ or cost$ or measur$ or disease$ or mean or gain or gains or index$)).ti,ab,kf. (40187)
101 utilities.ti,ab,kf. (17921)
102 (eq-5d or eq5d or eq-5 or eq5 or euro qual or euroqual or euro qual5d or euroqual5d or euro qol or euroqol or euro qol5d or euroqol5d or euro quol or euroquol or euro quol5d or euroquol5d or eur qol or euroqol or eur qol5d or eur?qul or eur?qul5d or euro$ quality of life or european qol).ti,ab,kf. (42446)
103 (euro$ adj3 (5 d or 5d or 5 dimension$ or 5dimension$ or 5 domain$ or 5domain$)).ti,ab,kf. (11916)
104 (sf36$ or sf 36$ or sf thirtysix or sf thirty six).ti,ab,kf. (54577)
105 (time trade off$1 or time tradeoff$1 or tto or timetradeoff$1).ti,ab,kf. (4284)
106 "quality of life"/ and ((quality of life or qol) adj (score$1 or measure$1)).ti,ab,kf. (42528)
107 "quality of life"/ and ec.fs. (78572)
108 "quality of life"/ and (health adj3 status).ti,ab,kf. (27203)
109 (quality of life or qol).ti,ab,kf. and "Cost Benefit Analysis"/ (7952)
110 ((qol or hrqol or quality of life).ti,kf. or *quality of life/) and ((qol or hrqol$ or quality of life) adj2 (increas$ or decrease$ or improv$ or declin$ or reduc$ or high$ or low$ or effect or effects or worse or score or scores or change$1 or impact$1 or impacted or deteriorat$)).ab. (99158)
111 "cost benefit analysis"/ and (cost-effectiveness ratio$ and (perspective$ or life expectanc$)).ti,ab,kf. (1496)
112 *"quality of life"/ and (quality of life or qol).ti. (141261)
113 "quality of life"/ and ((quality of life or qol) adj3 (improv$ or chang$)).ti,ab,kf. (142151)
114 "quality of life"/ and health-related quality of life.ti,ab,kf. (101963)
115 economic model/ (4580)
116 or/94-115 (542677)
117 61 and 80 (4)
118 61 and 93 (4)
119 61 and 116 (7)
120 117 or 118 or 119 (11)

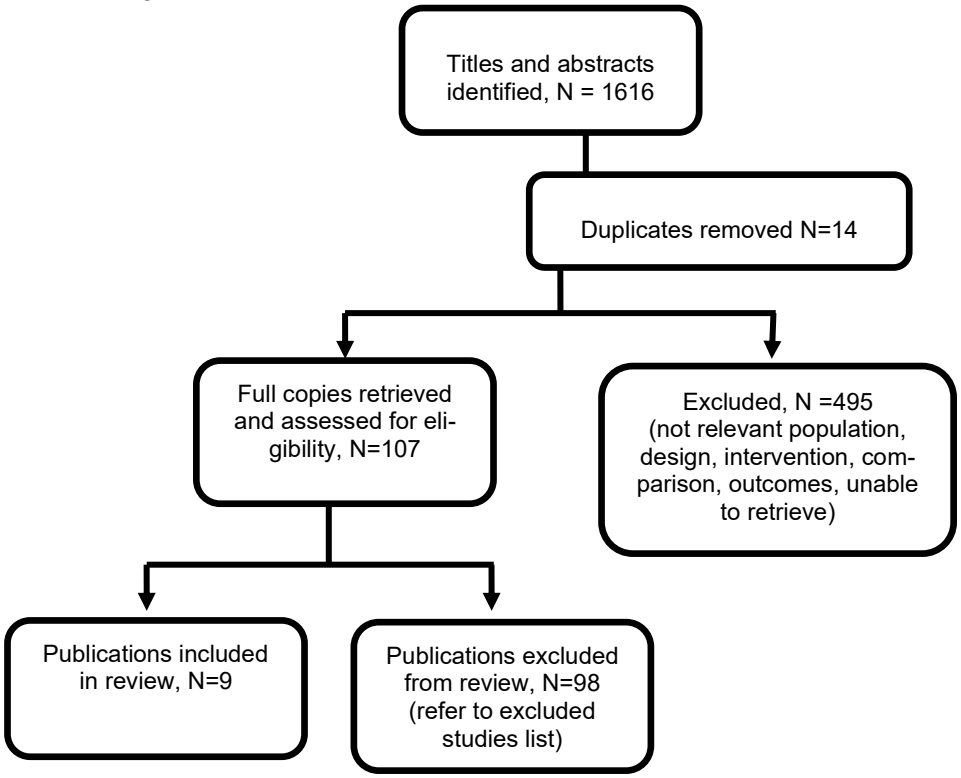
Database name: INAHTA

Searches
1 "Epilepsy, Rolandic"[mh] (0)
2 ((bcects or bects or brec))[Title] OR ((bcects or bects or brec))[abs] (0)
3 ((benign* AND epilep*))[Title] OR ((benign* AND epilep*)) (1)
4 (((benign AND child*) AND (convuls* or epilep* or seizure* or spasm*)))[Title] OR (((benign AND child*) AND (convuls* or epilep* or seizure* or spasm*)))[abs] (1)
5 (((benign AND neonat*) AND (convuls* or epilep* or seizure* or spasm*)))[Title] OR (((benign AND neonat*) AND (convuls* or epilep* or seizure* or spasm*)))[abs] (0)
6 (((benign AND paediatric*) AND (convuls* or epilep* or seizure* or spasm*)))[Title] OR (((benign AND paediatric*) AND (convuls* or epilep* or seizure* or spasm*)))[abs] (0)
7 (((benign AND pediatric*) AND (convuls* or epilep* or seizure* or spasm*)))[Title] OR (((benign AND pediatric*) AND (convuls* or epilep* or seizure* or spasm*)))[abs] (0)
8 (((convuls* or epilep*) AND (centrotemporal* AND spike*)))[Title] OR (((convuls* or epilep*) AND (centrotemporal* AND spike*)))[abs] (1)
9 (CECTS)[Title] OR (CECTS)[abs] (0)
10 (((centralopathic* or centrotemporal* or temporal-central) AND (convuls* or epilep* or seizure*)))[Title] OR (((centralopathic* or centrotemporal* or temporal-central) AND (convuls* or epilep* or seizure*)))[abs] (1)
11 (((sylvian* or postrolandic* or roland*) AND (convuls* or epilep* or seizure* or spasm*)))[Title] OR (((sylvian* or postrolandic* or roland*) AND (convuls* or epilep* or seizure* or spasm*)))[abs] (0)
12 #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1 (1) (Date limited to 2011 – 2026 (0)

Appendix C – Clinical evidence study selection

Clinical study selection for: What antiseizure medications (monotherapy or add-on) are effective in the treatment of self-limited epilepsy with centrotemporal spikes?

Figure 1: Study selection flowchart



Appendix D – Clinical evidence tables

Clinical evidence tables for review question: What antiseizure medications (monotherapy or add-on) are effective in the treatment of self-limited epilepsy with centrotemporal spikes?

Table 11: Clinical evidence tables

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
Full citation Ahadi, P., Nasiri, J., Ghazavi, M., Mosavian, T., Mansouri, V., A comparative study on the efficacy of levetiracetam and carbamazepine in the treatment of rolandic seizures in children: An open-label randomized controlled trial, Journal of Research in Pharmacy Practice, 9, 68-72, 2020 **Ref Id** 1291164. **Country/ies where the study was carried out** Iran. **Study type** Randomised con-	**Sample size** N=92. Levetiracetam n=46; carbamazepine n=46. **Characteristics** Children with a clinical diagnosis of benign childhood epilepsy with centro temporal spikes and an EEG showing characteristics of rolandic epilepsy. Sex: Male - levetiracetam n=26; carbamazepine n=28, female - levetiracetam n=20; carbamazepine n=18, p=0.832. Age, years, mean (SD): levetiracetam 8.7 (2.766); carbamazepine 8.36 (2.250), p=0.514. Weight, kg,	**Interventions** Levebel (levetiracetam) oral solution 100 mg/ml at initial dose of 25-30 mg/kg/day versus tegretol (carbamazepine) syrup 20 mg/ml at initial dose of 15-20 mg/kg/day. The levetiracetam and carbamazepine dosages ranged from 27.07 to 31.57 mg/kg/daily and from 12.78 to 13.13 mg/kg/daily (differences due to rounding the amount of daily prescribed drug), respectively.	**Details** Consecutive selection of patients referred to paediatric neurology department at one hospital. Computer generated random numbers. Participants who had a severe reaction to either treatment were excluded from the study and treated with other medications. Open label/participants and investigators were not blinded to treatment allocation. Seizure freedom defined as absence of seizures for at least 1 month. Follow-up by a paediatric neurologist took place every 2 months for a period of 6 months after the start of treatment.	**Results** **Critical outcomes** Seizure freedom at 6 months: Levetiracetam n=47/47; carbamazepine n=47/47. Adverse events – leading to change in medication: levetiracetam n=1/47; carbamazepine n=1/47. NB. Authors report that decreased appetite was most common adverse event. These two patients were excluded from the study.	**Limitations** Methodological limitations assessed using the Cochrane risk of bias tool for randomised trials (Version 2.0) **Domain 1: Randomisation: Some concerns** 1.1: Yes, computer generated randomisation. 1.2: No information is provided regarding concealment of allocation however it is unlikely that the enrolling investigator or the participant had knowledge of the forthcoming allocation. 1.3: No, there were no significant differences between groups at baseline.

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
trolled trial. **Aim of the study** To "... investigate whether levetiracetam should be preferred to carbamazepine as a treatment choice for benign childhood epilepsy with centro Temporal spikes ..." p 68 **Study dates** 2018 - 2020. **Source of funding** Isfahan University of Medical Sciences (Project Number: 398460).	mean (SD): levetiracetam 28.45 (9.306); carbamazepine 28.72 (8.754), p=0.882. Seizure frequency before starting treatment (mean): 1 per month. **Inclusion criteria** • More than two attacks per year. • Normal MRI. • Between the ages of 4 and 12 years. **Exclusion criteria** • 'Under' multi drug therapy. • A history of severe side effects or reaction to levetiracetam or carbamazepine.		Frequency and duration of seizures and side effects recorded using a predesigned checklist. Follow-up: 6 months (no measure of variability was reported)		**Domain 2: Deviations from intended interventions: Some concerns** 2.1: Yes, participants were aware of their treatment allocation. 2.2: Yes, carers and those delivering interventions were aware of treatment allocation. 2.3 Probably no, changes to the intervention occurred due to adverse events which is consistent with trial protocol. 2.6 Probably no, patients who changed treatments due to adverse events were excluded from final analysis of some outcome data. 2.7 Probably no, it is unlikely that the exclusion of data from patients who changed treatments due to adverse events would have had a substantial effect on the results. **Domain 3: Missing outcome data: Low risk**

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
					3.1: Probably yes, although missing outcome data is not reported on specifically, it appears that data were available for all outcomes and participants (with the exception of those excluded from the final analysis due to adverse event related treatment cessation. **Domain 4: Measurement of the outcome: Low risk** 4.1: No, methods of outcome measurement are appropriate. 4.2: No, measurement of the outcome is unlikely to have differed between intervention groups. **Domain 5: Selection of the reported result: Some concerns** 5.1: No information, analysis plans are not reported in sufficient detail to enable assessment although it is unlikely that selective reporting due to unblinded outcome data was an issue.

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
					5.2: No information, analysis plans are not reported in sufficient detail to enable assessment, and there is more than one way in which the outcome domain could have been measured. 5.3 No information, analysis plans are not available, however it is unlikely that selective reporting of analyses was an issues **Domain 6: Overall judgment of bias: High risk.** The study is judged to have some concerns for multiple domains in a way that substantially lowers confidence in the result.
Full citation Borggraefe, I., Bonfert, M., Bast, T., Neubauer, B. A., Schotten, K. J., Maßmann, K., Noachtar, S., Tuxhorn, I., May, T. W., Heinen, F., Levetiracetam vs. sulthiame in benign epilepsy with centrotemporal spikes in childhood: a double-blinded, randomized, controlled	**Sample size** Total recruited: N = 44 Analysis conducted: N = 43 Levetiracetam (n=21), Sultiame (n=22) **Characteristics** Mean age Levetiracetam: 8.7 years (SD 1.7), Sultiame: 9.0 years (SD	**Interventions** Levetiracetam Starting dose: 10mg/kg body weight (weekly increments of 10mg/kg body weight) Final dose: 30mg/kg body weight Sultiame Starting dose: 2mg/kg body weight (weekly	**Details** Medication which looked the same for both treatments was produced by Haupt Pharma Wuelfing, Germany Outcomes were assessed at baseline, after 4 weeks, 12 weeks, and 27 weeks	**Results** **Critical outcomes** Occurrence of treatment failure (occurrence of a seizure in the 24 week observation period after reaching target dose) Levetiracetam: n=4 (19.0%) Sultiame: n=2 (9.1%).	**Limitations** Methodological limitations assessed using the Cochrane risk of bias tool for randomised trials (Version 2.0) **Domain 1: Randomisation: Low risk** 1.1: Yes, patients were randomly allocated to treatments

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
trial (German HEAD Study), European journal of paediatric neurology: EJPN, 17, 507-514, 2013 **Ref Id** 1082298 **Country/ies where the study was carried out** Germany **Study type** Multi-centre double blind randomized controlled trial **Aim of the study** To determine the efficacy, tolerability and safety of levetiracetam and sultiame in participants with Benign childhood epilepsy with centrotemporal spikes (BECTS) **Study dates** 2006 to 2008 **Source of funding** The study was part funded by UCB Pharma SA, Brussels, Belgium	1.5) Number of females Levetiracetam: n=6 (28.6%), Sultiame: n=10 45.5%) Mean number of seizures (before study entry) Levetiracetam: 6.4 (SD 8.3), Sultiame: 5.2 (SD 10.2) No statistically differences seen between the treatment groups (p values not provided) **Inclusion criteria** • Male and female participants • Aged between 6 and 12 years • Diagnosed with BECTS, who had experienced two or more seizures within the past 6 months **Exclusion criteria**	increments of 2mg/kg body weight) Final dose: 6mg/kg body weight Down dosing to 20mg/kg (Levetiracetam) or 4mg/kg (Sultiame) body weight was allowed in case of adverse events	(end of observation period) After an observation period of 24 weeks, the study was unblinded and participants could choose to continue treatment or not. Data analysed according to intention to treat Follow-up: 27 weeks (no measure of variability was reported)	<u>Serious adverse event, leading to treatment dropout</u> Levetiracetam: n= 5 (23.8%) Sultiame: n= 1 (4.5%)	1.2: Yes, randomisation was conducted in a central randomisation centre using permuted blocks 1.3: No, no significant differences between groups at baseline **Domain 2: Deviations from intended interventions: Low risk** 2.1: No, double blind study 2.2: No, double blind study **Domain 3: Missing outcome data: Low risk** 3.1: Yes, only data from one participant was not included in the analysis **Domain 4: Measurement of the outcome: Low risk** 4.1: No information, outcomes clearly defined, but no information was provided on how they were assessed, or by whom 4.2: Probably no, outcomes included seizure occurrence and ad-

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
	• Coincidence of other epilepsy forms • Participation in another clinical study (within 30 days prior to study starting) • Mental retardation				verse events, unlikely to differ between treatment arms 4.3: No, double blind study **Domain 5: Selection of the reported result: Some concerns** 5.1: No, the study did not meet the required number of participants to conduct the planned analysis 5.2: No, descriptive data presented 5.3: No, data presented as expected **Domain 6: Overall judgment of bias: Some concerns** The study did not recruit the 120 sample size needed for the primary outcome - leading to overall bias result
Full citation Coppola, G., Franzoni, E., Verrotti, A., Garone, C., Sarajlija, J., Operto, F. F., Pascotto, A., Levetiracetam or oxcarbazepine as monotherapy in newly diagnosed benign epilepsy	**Sample size** Total recruited: N= 39 Levetiracetam: n=21 Oxcarbazepine: n= 18 **Characteristics** Mean age	**Interventions** Levetiracetam and Oxcarbazepine Starting dose: 5mg/kg, with 3 day incremental increase of 5mg/kg Final dose: 20mg/kg	**Details** In case of seizure recurrence daily does of Levetiracetam could be increased to 30mg/kg In case of seizure recurrence, the daily dose of Oxcarbazepine could be increased to	**Results** **Critical outcomes** Seizure freedom (18 months) Levetiracetam: n=19 (90.5%), Oxcarbazpine: n = 13 (72.2%) Adverse events leading	**Limitations** Methodological limitations assessed using the Cochrane risk of bias tool for randomised trials (Version 2.0) **Domain 1: Randomisation: Some con-**

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
of childhood with centrotemporal spikes (BECTS): An open-label, parallel group trial, Brain and Development, 29, 281-284, 2007 **Ref Id** 1082322 **Country/ies where the study was carried out** Italy **Study type** Open label pilot study **Aim of the study** To determine the efficacy and tolerability of levetiracetam and oxcarbazepine for participants with benign epilepsy with centrotemporal spikes **Study dates** Not stated **Source of funding** Not stated	Levetiracetam: 10.5 years, oxcarbazepine: 8.4 years Number of females Levetiracetam: n=10 (41.6%), oxcarbazepine: n=8 (44.4%) Mean number of seizure (during baseline period) Levetiracetam: 1.8 seizures/month, oxcarbazepine: 1.5 seizures/month **Inclusion criteria** • Males and females • Aged 3 to 12 years • Newly diagnosed with BECTS (according to LIAE classification) • Frequent seizures in the last 6 months (seizures to occur during wakefulness) • Partial motor seizures (hemifacial or hemiclonic) with or without generalisation		35mg/kg Data analysed according to intention to treat Mean follow-up (range): 18.5 (12–24) months	<u>to withdrawal of medication</u> Levetiracetam: n=1/21, Oxcarbazpine: n = 1/18 <u>Adverse events (not leading to withdrawal)</u> Levetiracetam: n=2/21, Oxcarbazpine: n = 1/18	**cerns** 1.1: Yes, children were randomised 1.2: No information, no details on allocation concealment provided 1.3: Probably yes, baseline characteristics given, no statistical data provided but there appear to be some differences; however, children were matched so this may not be an issue **Domain 2: Deviations from intended interventions: Some concerns** 2.1: Yes, an open label pilot study 2.2: Yes, an open label pilot study 2.3: No information, no details provided about deviations from the protocol **Domain 3: Missing outcome data: Low risk** 3.1: No information, no details provided on missing data 3.2: Probably yes, in-

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
	• EEG features of peculiar focal or multifocal centrotemporal spikes • MRI with normal or slight abnormal results • absence of neurological and mental deficits • No previous therapy • Provided informed consent **Exclusion criteria** • Poor compliance by parents or caregivers to complete seizure diary • progressive neurological and or systemic disease • Those with associated pseudoseizures during MRI scan				tention to treat analysis was carried out **Domain 4: Measurement of the outcome: Some concerns** 4.1: Probably no, outcome data recorded in diaries by parents/carers 4.2: Probably no, data collected methods consistent across arms 4.3: Yes, open label pilot study 4.4: Probably yes, data recorded by parents/carers; therefore, knowledge of medication could lead to bias 4.5: No information, unclear what information parents/carers were given about the treatment; therefore, it is difficult to determine if their beliefs about the medication influenced recording of data **Domain 5: Selection of the reported result: Low risk** 5.1: Probably yes, Study states ITT analysis conducted

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
					5.2: No, data provided as expected 5.3: No, data provided as expected **Domain 6: Overall judgment of bias: Some concerns**
Full citation Kang, H. C., Eun, B. L., Wu Lee, C., Ku Moon, H., Kim, J. S., Wook Kim, D., Soo Lee, J., Young Chae, K., Ho Cha, B., Sook Suh, E., et al., The effects on cognitive function and behavioral problems of topiramate compared to carbamazepine as monotherapy for children with benign rolandic epilepsy, Epilepsia, 48, 1716-1723, 2007 **Ref Id** 1082380 **Country/ies where the study was carried out** Korea **Study type** Multi-centre, open label randomised trial	**Sample size** Total enrolled: N=112 Topiramate: n=58, Carbamazepine: n=54 Total completed: n=88 **Characteristics** Mean age Topiramate: 8.7 years (SD 1.9), Carbamazepine: 8.7 years (SD 2.0) Number of females Topiramate: n=26 (44.8%), Carbamazepine: n=22 (40.7%) **Inclusion criteria** • Normal intelligence • Aged 5 to 15 years • Had at least 2 partial seizures during 6 months at baseline • Clinical and EEG findings compatible	**Interventions** <u>Topiramate</u> Starting dose: 12.5mg/day, incremental increases over 4 weeks Final dose of at least 50mg/day if weighed under 30kg, or at least 75mg/day if weighed over 30kg <u>Carbamazepine</u> Starting dose: 10mg/kg/day, incremental increases over 4 weeks Final dose of at least 20/kg/day	**Details** The study had a baseline 6 month phase followed a one week screening phase to determine eligibility And a four week dose escalation phase, and a 6 week maintenance phase where dose was kept stable Average daily dose during the maintenance phase was 3.4mg/kg/day TPM and 21.6mg/kg/day CBZ Follow-up: 28 weeks (no measure of variability reported)	**Results** **Critical outcomes** <u>Seizure free (mean follow-up 28 weeks)</u> Topiramate: n=40, Carbamazepine: n=38 <u>Number of patients who experienced an adverse event (follow-up mean 28 weeks)</u> Topiramate: n=16/58 Carbamazepine: n=19/54 <u>Number of patients who withdrew due to adverse events</u> Topiramate: n=6/58 Carbamazepine: n=5/54	**Limitations** <u>Methodological limitations assessed using the Cochrane risk of bias tool for randomised trials (Version 2.0)</u> **Domain 1: Randomisation: Some concerns** 1.1: Yes, each study center had a randomisation plan 1.2: No information, no details provided on concealment of allocation 1.3: Probably no, no clearly reported differences at baseline; however, no p values provided so difficult to be certain **Domain 2: Deviations from intended interventions: Low risk** 2.1: Yes, an open label

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
Aim of the study To determine the cognitive and behavioural effects of Topiramate (TPM) as compared to carbamazepine (CBZ) in children with benign Rolandic epilepsy **Study dates** Not stated **Source of funding** The study was supported by a grant from Janssen, Korea limited, a Johnson and Johnson company	with benign Rolandic epilepsy • Plus, at least one of the following: • Parent or patient wanted to take ASM • daytime seizures • at least 1 episode of a convulsive seizure during 6 months at baseline **Exclusion criteria** • Evidence of progressive cerebral lesion • Neurodegenerative metabolic disorder • Cognitive impairment that could interfere with cognitive testing • History of psychiatric disorder requiring tranquilizers in the past 6 months • Regular use of antihistamines or CNS active compounds in the past 6 months • History of poor drug compliance				study, only the observer was blinded 2.2: Probably no, states that the observer is blinded, but no details given 2/3: Probably no, no deviations from the intended protocol were reported **Domain 3: Missing outcome data: Low risk** 3.1: Probably no, drop-outs are reported, and data analysis conducted as intention to treat 3.2: Probably yes, Intention to treat analysis conducted **Domain 4: Measurement of the outcome: Low risk** 4.1: Probably no, outcomes measured using validated tools 4.2: Probably no, same tools used across the groups 4.3: No, observers were blind to treatment **Domain 5: Selection of the reported result:**

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
	• Inability to maintain a seizure calendar • History of nephrolithiasis • Previously treated with TPM or CBZ				**High risk** 5.1: probably yes, data analysis described 5.2: Probably yes, a number of tools were used to assess neuropsychological outcomes, data was unclearly reported making interpretation difficult 5.3: No information: Data on neuropsychological outcomes was unclearly reported making interpretation difficult **Domain 6: Overall judgment of bias: High risk** **Other information** Some data were presented in a way that could not be extracted (this is, change in seizure frequency and neuropsychological test results)
Full citation Kwon, Soonhak, Hwang, Tae Gyu, Lee, Junhwa, Kim, Doo-Kwun, Seo, Hye-Eun, Benign childhood epilepsy with centrotem-	**Sample size** N=39 randomised. Intervention group n=13 Control n=16	**Interventions** Intervention group: Oxcarbazepine initially administered once or twice a day at a dose of 5-10 mg/kg/day and	**Details** The study consisted of screening, randomization and a 30 week treatment phase. Each center was given a	**Results** **Primary outcomes** Seizure freedom (6 months) Intervention group n=7/13; control group	**Limitations** Methodological limitations assessed using the Cochrane risk of bias tool for randomised trials (Version 2.0)

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
poral spikes: to treat or not to treat, Journal of epilepsy research, 3, 1-6, 2013 **Ref Id** 1310611 **Country/ies where the study was carried out** South Korea **Study type** Randomised controlled trial (multi-centre) **Aim of the study** To determine the "…the benefits and risks of oxcarbazepine (OXC) monotherapy as a first-line AED in children with newly diagnosed BCECT were evaluated based on clinico-electrical and neuro-psychological findings over time." p 1 **Study dates** Not reported **Source of funding** Novartis Korea	**Characteristics** Childern with newly diagnosed, benign partial epilepsy recruited from 4 tertiary medical centers functioning as referral centres in 4 different regions of South Korea. Age, mean, years: intervention group 8.2 ±2.3; control group 8.5±2.3. Sex: Intervention group male n=6, female n=7; control group male n=11; female n=8. **Inclusion criteria** • Aged between 5 and 15 years • 2 or more seizures over the past 6 months • Diagnosed with BECTS by pediatric neurologists. **Exclusion criteria** • Primary generalised seizures • Partial epilepsies of a	titrated to 10-20 mg/kg/day over a week. This allowed dosages to be increased to a therapeutic range if the patients experienced increased frequency or severity of seizures in comparison to baseline. Control group: No treatment.	separate and independent randomization protocol using a random code assignment. EEGs read by 2 or more experienced specialists. Location and frequency of spikes were quantified for each patient. Spike index was calculated by dividing the total number of spikes by the total time the patient was evaluated. Full-scale intelligence quotient derived from scores on Korean versions of Wechsler Intelligence Scale for Children III. Follow-up: 6 months (no measure of variabil-ity reported)	n=8/16. Reduction of seizure frequency >50% Intervention group n=3/13; control group n=3/16. **Secondary outcomes** Normalisation of sleep EEG (6 months) Intervention group n=2/13; control group n=3/16. EEG spike index - left (6 months, frequency/minute): Intervention group 26.2±18.0; control group 11.8±20.0. EEG spike index - right (6 months, frequency/minute): intervention group 19.1±18.4; control group 3.8±7.9. Full-scale intelligence quotient (6 months): intervention group 97.6±7.5; control group 111.4±18.6.	**Domain 1: Randomisation: Low risk** 1.1: Yes, each centre had a randomisation protocol 1.2: Yes. Randomisation protocol provided by external agency. 1.3: Probably no. Only minimal demographic data provided however baseline values for clinical data are also provided and these do not suggest that any issues with randomisation arose. **Domain 2: Deviations from intended interventions: Low risk** 2.1: Yes. Participants were aware of their assigned intervention. 2.2: Yes. Parents/carers and individuals delivering the interventions were aware of assigned interventions. 2.3: Probably no. No deviations are reported and any that arose would be unlikely to do so as a result of the trial context. 2.6: Yes. An an appro-

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
	symptomatic Etiology • Neurodegenerative conditions • History of psychiatric conditions • History of taking antiepileptic drugs over previous 3 months.			Although baseline values for all outcomes are reported insufficient data is reported to allow presentation of change scores.	priate analysis was used. **Domain 3: Missing outcome data: Low risk** 3.1: Yes. Outcome data available for all patients. **Domain 4: Measurement of the outcome: Some concerns** 4.1: No. Method of measuring outcome was appropriate. 4.2: No. Measurement of the outcome did not differ between intervention groups. 4.3: No information. No details provided regarding blinding of outcome assessors. 4.4: Probably yes. Outcome assessment ssessment could be influenced by knowledged of the intervention received. 4.5: Probably no. It is unlikely that assessment of the outcome was influenced by knowledge of intervention received.

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
					Domain 5: Selection of the reported result: Some concerns 5.1: No information. Analysis plans not provided. 5.2: No information. Analysis plans are not provided. 5.3: No information. Analysis plans not provided. **Domain 6: Overall judgment of bias: Some concerns.** **The study is judged to raise some concerns in at least one domain for this result, but not to be at high risk of bias for any domain.**
Full citation Mitsudome, A., Ohfu, M., Yasumoto, S., Ogawa, A., Hirose, S., Ogata, H., Yamada, T., The effectiveness of clonazepam on the Rolandic discharges, Brain and Development, 19, 274-278, 1997	**Sample size** EEG Total: N= 40 Clonazepam (CZP): n=20 Valproate (VPA): n=10 Carbamazepine (CBZ): n=10 **Characteristics** Mean age	**Interventions** Dose of clonazepam: 0.35-1.0mg/day Dose of valproate: 250-600mg/day Dose of carbamazepine: 100-200mg/day	**Details** The first EEG was recorded before administration of drug, the second after 4 weeks of medication Follow-up: 4 weeks (no measure of variability reported)	**Results** **Important outcomes** Disappearance of Rolandic discharge on EEG Clonazepam: n=15 (75%) Valproate: n=1 (10%) Carbamazepine: n=0 (0%)	**Limitations** Methodological limitations assessed using the Cochrane risk of bias tool for randomised trials (Version 2.0) **Domain 1: Randomisation: High risk** 1.1: Yes, children were randomly sorted

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
Ref Id 1082416 **Country/ies where the study was carried out** Japan **Study type** Randomised controlled trial **Aim of the study** To determine the effect of Clonazepam compared to Valproate and Carbamazepine on Rolandic discharge on Electroencephalography (EEG) **Study dates** Not stated **Source of funding** Not stated	CZP: 7.3 years (range 3.11 to 9.11), VPA: 8.6 years (range 4.0 - 10.11), CBZ: 8.6 years (range 5.5 - 10.3) Number of females CZP: n=9 (45%0, VPA: n=4 (40%), CBZ: n= 5 (50%) **Inclusion criteria** • Newly diagnosed with benign epilepsy in childhood with centrotemporal spikes (BECTS) • With typical Rolandic discharge of EEG • Not treated for BECTS prior to study **Exclusion criteria** • None stated				1.2: No information, no details provided on allocation concealment 1.3: Probably yes, no baseline differences between groups were demonstrated; however, double the number of participants were allocated to the clonazepam group **Domain 2: Deviations from intended interventions: Some concerns** 2.1: No information 2.2: No information 2.3: No information **Domain 3: Missing outcome data: High risk** 3.1: No information, no details on missing data provided 3.2: Probably no, no information, unequal balance of participants in the arms may indicated bias in the research 3.3: No information 3.4: No information **Domain 4: Measure-**

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
					ment of the outcome: High risk 4.1: No, outcome data measured by EEG, and two investigators agreed the reading 4.2: Probably no, data collection methods consistent across arms 4.3: No information 4.4: Probably yes, potential bias of observer could influence their reading of the EEG 4.5: No information **Domain 5: Selection of the reported result: Some concerns** 5.1: No information, no data analysis plan provided 5.2: No, EEG readings provided as expected 5.3: No, decision on EEG data provided as expected. **Domain 6: Overall judgment of bias: High risk** **Other information** Brief publication with little detail on methods

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
Full citation Rating, D., Wolf, C., Bast, T., Sulthiame as monotherapy in children with benign childhood epilepsy with centrotemporal spikes: A 6-month randomized, double-blind, placebo-controlled study, Epilepsia, 41, 1284-1288, 2000 **Ref Id** 1082446 **Country/ies where the study was carried out** Germany **Study type** Double-blind, placebo randomised trial **Aim of the study** To determine the efficacy of Sultiame in preventing seizures in children with Benign childhood epilepsy with centrotemporal spikes (BECTS) **Study dates** 1996 to 1999	**Sample size** Total randomised: N=66. Sultiame: n=31, placebo: n= 35 **Characteristics** Mean age Sultiame: 8 years (range 3-10), placebo: 8 years (range 3-10) Number of females Sultiame: n=15 (48.4%), placebo: n=11 (31.4%) Total number of seizures prior to study date Sultiame: n=4 (range 2-20), placebo: n=3 (range 2-80) **Inclusion criteria** • Diagnosed with BECTS • Had 2 or more seizures in the past 6 months • Aged between 3 and 10 years	**Interventions** **Sultiame** 5mg/kg/day given in three administrations per day Relative dose administered varied from 3.1 to 5.7mg/kg/day	**Details** Patients assessed at screening, day 14, day 28, and at 3 and 6 months Follow-up: 6 months (no measure of variability was reported)	**Results** **Critical outcomes** Treatment failure (defined as no seizure in first 7 days, no adverse event or withdrawal Sultiame: n=6, placebo: n=25 **Important outcomes** EEG awake, Specific pathology (follow-up mean 6 months) Sultiame: n= 10/25, placebo: n=5/10 EEG awake, normal - EEG (follow-up mean 6 months) Sultiame: 11/25, placebo: 2/10. EEG sleep, specific pathology (follow-up mean 6 months) Sultiame: 10/25, placebo: 6/10. EEG sleep, normal - (follow-up mean 6 months) Sultiame: 10/25, placebo: 1/10.	**Limitations** Methodological limitations assessed using the Cochrane risk of bias tool for randomised trials (Version 2.0) **Domain 1: Randomisation: Low risk** 1.1: Yes, participants randomized into blocks of four using a prepared list. 1.2: Yes, the randomisation codes were in sealed envelopes. 1.3: Yes, there were no significant differences between the groups at baseline. **Domain 2: Deviations from intended** interventions: Low risk 2.1: Probably no, the study states it was double blind; however, no details are provided 2.2: Probably no, the study states it was double blind; however, no details are provided **Domain 3: Missing outcome data: Low risk**

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
Source of funding Not stated	**Exclusion criteria** • Presence of severe organic disease • acute porphyria • somatic signs of puberty • relevant hypersensitivity • history of mental illness • relevant renal, thyroid or hepatic dysfunction				3.1: Yes, the paper reports dropouts and data presented for the time period of the study, data on EEG is missing in placebo group over time. **Domain 4: Measurement of the outcome: Low risk** 4.1: No information, the outcome "treatment failure" was defined but there was no information on how this was assessed. 4.2: No 4.3: Probably no, the study claims to be double blind **Domain 5: Selection of the reported result: Low risk** 5.1: Probably yes, the data analysis was described, with ITT at interim time point once 60 participants recruited 5.2: No, only one set of measurements for outcomes **Domain 6: Overall**

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
					judgment of bias: Low risk
Full citation Suo, G. H., Zheng, Y. Q., Wu, Y. J., Tang, J. H., Effects of levetiracetam and oxcarbazepine monotherapy on intellectual and cognitive development in children with benign epilepsy with centrotemporal spikes, Acta Neurologica Belgica, 2021 **Ref Id** 1310603 **Country/ies where the study was carried out** China. **Study type** Randomised controlled trial. **Aim of the study** To "…the efficacy of LEV and OXC monotherapy for the treatment of children with BCECTS, and the effect of these treatments on intelligence and cognitive development …" p 2	**Sample size** N=70 randomised (n=64 completed/analysed). Intervention group n=35 randomised (n=32 completed/analysed). Control group n=35 (n=32 completed/analysed). **Characteristics** Children diagnosed with BECTS in the outpatient department of the Affiliated Hospital of Nantong University. **Inclusion criteria** Age, years: Intervention group 8.47 ± 2.13; control group 8.62 ± 2.21, p = 0.783 Age at onset, years: Intervention group 6.98 ± 1.82; control group 7.13 ± 1.75, p = 0.738 Gender, male, (%): Intervention group n=21	**Interventions** Intervention: Levetiracetam – 250 mg tablets (Keppra). Initial dose set at 10 mg/kg/day. Dose increased once every 7 days and maintained at 20–60 mg/kg/day. Control: Oxcarbazepine – 150 mg tablets. Initial dose set at 8–10 mg/kg/day, orally administered twice a day at an interval of 12 hours. Dose increased to 5–10 mg/kg/day every 5–7 days and maintained at 20–46 mg/kg/day. All children started treatment at a low dose and returned to the clinic for assessment once a week at the beginning of treatment. During the treatment, clinical reactions in each child were closely observed, and the dosage of drug was appropriately adjusted according to the weight	**Details** 1:1 randomisation. Follow-up at 1, 3, and 6 months. No information provided regarding handling of missing data. Follow-up: 6 months (no measure of variability was reported)	**Results** Seizure freedom (3 months): Intervention group n=12/32; control group n=16/32. Seizure freedom (6 months): Intervention group n=17/32; control group n=25/32. EEG – normal (3 months): Intervention group n=10/32; control group n=13/32. EEG – normal (6 months): Intervention group n=14/32; control group n=19/32. Adverse events – number of patients experiencing any adverse event (timescale not reported): Intervention group n=6/32; control group	**Limitations** Methodological limitations assessed using the Cochrane risk of bias tool for randomised trials (Version 2.0) **Domain 1: Randomisation: Low risk** 1.1: Yes. Random number table. 1.2: No information. No details on allocation concealment are reported. 1.3: No. No significant differences at baseline. **Domain 2: Deviations from intended interventions**: Some concerns 2.1: No information. Not clear whether particiapnts were aware of assigned interventions. 2.2: No information. Not clear carers or those delivering were aware of assigned interventions. 2.3: Probably no. Deviations not reported clearly however any

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
Study dates October 2018 – February 2020. **Source of funding** Suzhou Science and Technology Plan (People's Livelihood Science and Technology), the Scientific Research Project of Jiangsu Health Commission, and the Nantong Science and Technology Project.	(65.63); control group n=19 (59.38), *p* = 0.606 **Inclusion criteria** • diagnosis of BECTS according to 2017 ILAE criteria • EEG features showing that seizure during an epileptic attack was partial or was generalised to the whole body and that the background rhythm was normal • at least 2 convulsions before recruitment • no abnormality in head MRI or CT examination • normal liver and kidney function prior to commencement of medication. **Exclusion criteria** • Encephalitis, brain injury, cerebralhemorrhage, and other organic diseases of the nervous system • functional insufficiency of the liver, lung, kidney or other important organs • emergence of mental	of the child and his/her seizure status. If a child exhibited obvious adverse events, the treatment was adjusted.		n=7/32.	arising would not be likely to do so as a result of the trial context. 2.6: No. Participants lost to follow-up/those who discontinued have been excluded from final analysis. 2.7: Probably no. Exclusion of these patients is unlikely to have influenced the results. **Domain 3: Missing outcome data: Low risk** 3.1: No. Six patients were excluded from analyses due to discontinuation/loss to follow-up. 3.2: No. No details regarding sensitivity analyses or methods to correct for missing outcome data are reported. 3.3 Probably no. Unlikely that missingness in outcome data depends on true value. **Domain 4: Measurement of the outcome: Low risk** 4.1: Yes. Methods of outcome measurement

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
	'retardation' • presence of cranial space-occupying lesions • poor medication compliance • any relevant drug contraindications.				are appropriate. 4.2: No. Unlikely to have differed between groups. 4.3: No information. Not clear whether outcome assessors were blinded. 4.4: Probably no. Assessment of the outcome unlikely to have been influenced by knowledge of interventions received. **Domain 5: Selection of the reported result: Some concerns** 5.1: No information. Pre-specified data analysis intentions not reported. 5.2: No information. Pre-specified data analysis intentions not reported. 5.3: No information. Pre-specified data analysis intentions not reported. **Domain 6: Overall judgment of bias: Some concerns.** The study is judged to raise some concerns in

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
					at least one domain for this result, but not to be at high risk of bias for any domain. **Other information** A number of scales relating to intelligence and cognitive function are reported however no summary outcome is reported and as these each relate to very specific components of intelligence and cognition these results have not been extracted.
Full citation Tacke, M., Borggraefe, I., Gerstl, L., Heinen, F., Vill, K., J et al., Effects of Levetiracetam and Sulthiame on EEG in benign epilepsy with centrotemporal spikes: A randomized controlled trial, Seizure, 56, 115-120, 2018 **Ref Id** 1082470 **Country/ies where the study was carried out** Germany	**Sample size** see Borggraefe 2013 **Characteristics** see Borggraefe 2013 **Inclusion criteria** see Borggraefe 2013 **Exclusion criteria** see Borggraefe 2013	**Interventions** see Borggraefe 2013	**Details** see Borggraefe 2013	**Results** **Important outcomes** Absence of EEG discharges in all available EEGs (27 weeks) Levetiracetam: n=8/13 Sultiame: n=11/21	**Limitations** see Borggraefe 2013 **Other information** see Borggraefe 2013

Study details	Participants	Interventions	Methods	Outcomes and results	Comments
Study type see Borggraefe 2013 **Aim of the study** To compare the effects of Levetiracetam and Sultiame on EEG in benign childhood epilepsy with centrotemporal spikes (BECTS) - secondary publication from the HEAD study (Borggraefe 2013) **Study dates** see Borggraefe 2013 **Source of funding** see Borggraefe 2013					

1

2

Appendix E – Forest plots

Forest plots for review question: What antiseizure medications (monotherapy or add-on) are effective in the treatment of self-limited epilepsy with centrotemporal spikes?

This section includes forest plots only for outcomes that are meta-analysed. Outcomes from single studies are not presented here, but the quality assessement for these outcomes is provided in the GRADE profiles in appendix F.

Comparison 3: levetiracetam versus oxcarbamazepine

Figure 2: adverse events

Appendix F – GRADE tables

GRADE tables for review question: What antiseizure medications (monotherapy or add-on) are effective in the treatment of self-limited epilepsy with centrotemporal spikes?

Table 12: Clinical evidence profile. Comparison 1: levetiracetam versus carbamazepine

Quality assessment							Number of patients		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	LEV	CBZ	Relative (95% CI)	Absolute	Quality	Importance
Seizure freedom at 6 months												
1 (Ahadi 2020)	RCT	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	47/47 (100%)	47/47 (100%)	RR 1.00 (0.96 to 1.04)	0 fewer per 1000 (from 40 fewer to 40 more)	⊕⊕OO LOW	CRITICAL
Adverse events – leading to change in medication												
1 (Ahadi 2020)	RCT	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/47 (2.1%)	1/47 (2.1%)	RR 1.00 (0.06 to 15.52)	0 fewer per 1000 (from 20 fewer to 309 more)	⊕OOO VERY LOW	CRITICAL

[1] *Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2*
[2] *Confidence interval crosses both MIDs (0.8 and 1.25)*

Table 13: Clinical evidence profile. Comparison 2: levetiracetam versus sultiame

Quality assessment	Number of patients	Effect	Quality	Importance

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	LEV	STM	Relative (95% CI)	Absolute		
Treatment failure (follow-up mean 24 weeks)												
1 (Borggraefe 2013)	RCT	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/21 (19%)	2/22 (9.1%)	RR 2.1 (0.43 to 10.26)	100 more per 1000 (from 52 fewer to 842 more)	⊕OOO VERY LOW	CRITICAL
Adverse event leading to withdrawal (follow-up mean 24 weeks)												
1 (Borggraefe 2013)	RCT	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	5/21 (23.8%)	1/22 (4.5%)	RR 5.24 (0.67 to 41.18)	193 more per 1000 (from 15 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Normal EEG (absence of EEG discharge at 27 weeks) (follow-up mean 27 weeks)												
1 (Tacke 2018)	RCT	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	8/13 (61.5%)	11/21 (52.4%)	RR 1.17 (0.65 to 2.12)	89 more per 1000 (from 183 fewer to 587 more)	⊕OOO VERY LOW	IMPORTANT

[1] *Serious risk of bias in the evidence contributing to the outcomes as per RoB 2*
[2] *Confidence intervals cross both MIDs (0.8 and 1.25)*

Table 14: Clinical evidence profile. Comparison 3: levetiracetam versus oxcarbazepine

Quality assessment							Number of patients		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	LEV	OXC	Relative (95% CI)	Absolute	Quality	Importance

Quality assessment							No of patients		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	LEV	OXC	Relative (95% CI)	Absolute	Quality	Importance
Seizure freedom (3 months)												
1 (Suo 2021)	RCT	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	12/32 (37.5%)	16/32 (50%)	RR 0.75 (0.43 to 1.32)	125 fewer per 1000 (from 285 fewer to 160 more)	⊕OOO VERY LOW	CRITICAL
Seizure freedom (6 months)												
1 (Suo 2021)	RCT	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	17/32 (53.1%)	25/32 (78.1%)	RR 0.68 (0.47 to 0.99)	250 fewer per 1000 (from 8 fewer to 414 fewer)	⊕⊕OO LOW	CRITICAL
Seizure freedom (18 months)												
1 (Coppola 2007)	RCT	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	19/21 (90.5%)	13/18 (72.2%)	RR 1.25 (0.91 to 1.72)	181 more per 1000 (from 65 fewer to 520 more)	⊕⊕OO LOW	CRITICAL
Adverse events												
2 (Coppola 2007, Suo 2021)	RCT	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	8/53 (15.1%)	8/50 (16%)	RR 0.97 (0.4 to 2.37)	5 fewer per 1000 (from 96 fewer to 219 more)	⊕OOO VERY LOW	CRITICAL
Adverse events leading to withdrawal of medication												
1 (Coppola 2007)	RCT	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/21 (4.8%)	1/18 (5.6%)	RR 0.86 (0.06 to 12.75)	8 fewer per 1000 (from 52 fewer to 653 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No of patients		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	LEV	OXC	Relative (95% CI)	Absolute	Quality	Importance
EEG normal (3 months)												
1 (Suo 2021)	RCT	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	10/32 (31.3%)	13/32 (40.6%)	RR 0.77 (0.4 to 1.49)	93 fewer per 1000 (from 244 fewer to 199 more)	⊕OOO VERY LOW	IMPORTANT
EEG normal (6 months)												
1 (Suo 2021)	RCT	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	14/32 (43.8%)	19/32 (59.4%)	RR 0.74 (0.45 to 1.2)	154 fewer per 1000 (from 327 fewer to 119 more)	⊕⊕OO LOW	IMPORTANT

1 Serious risk of bias in the evidence contributing to the outcomes as per RoB 2
2 Confidence interval crosses both MIDs (0.8 and 1.25)
3 Confidence interval crosses 1 MID (0.8 or 1.25)

Table 15: Clinical evidence profile. Comparison 4: topiramate versus carbamazepine

Quality assessment							Number of patients		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	TPM	CBZ	Relative (95% CI)	Absolute	Quality	Importance
Number of participants seizure free (mean follow-up 28 weeks)												
1	RCT	serious[1]	no serious	no serious	serious[2]	none	40/58	38/54	RR 0.98	14 fewer	⊕⊕OO	CRITICAL

Quality assessment							Number of patients		Effect		Quality	Importance
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	TPM	CBZ	Relative (95% CI)	Absolute		
(Kang 2007)			inconsistency	indirectness			(69%)	(70.4%)	(0.77 to 1.25)	per 1000 (from 162 fewer to 176 more)	LOW	
Number of patients who experienced an adverse event (follow-up mean 28 weeks)												
1 (Kang 2007)	RCT	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	16/58 (27.6%)	19/54 (35.2%)	RR 0.78 (0.45 to 1.36)	77 fewer per 1000 (from 194 fewer to 127 more)	⊕OOO VERY LOW	CRITICAL
Number of patients who withdrew due to adverse events (follow-up mean 28 weeks)												
1 (Kang 2007)	RCT	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	6/58 (10.3%)	5/54 (9.3%)	RR 1.12 (0.36 to 3.45)	11 more per 1000 (from 59 fewer to 227 more)	⊕OOO VERY LOW	CRITICAL

[1] *Serious risk of bias in the evidence contributing to the outcomes as per RoB 2*
[2] *Confidence interval crosses 1 MID (0.8 or 1.25)*
[3] *Confidence intervals cross both MIDs (0.8 and 1.25)*

Table 16: Clinical evidence profile. Comparison 5. oxcarbazepine versus no treatment

Quality assessment	Number of patients	Effect	Quality	Importance

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	OXC	No treat-ment	Relative (95% CI)	Absolute		
Seizure freedom (6 months)												
1 (Kwon 2013)	RCT	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	7/13 (53.8%)	8/16 (50%)	RR 1.08 (0.53 to 2.17)	40 more per 1000 (from 235 fewer to 585 more)	⊕OOO VERY LOW	CRITICAL
Reduction of seizure frequency > 50%												
1 (Kwon 2013)	RCT	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/13 (23.1%)	3/16 (18.8%)	RR 1.23 (0.3 to 5.11)	43 more per 1000 (from 131 fewer to 771 more)	⊕OOO VERY LOW	CRITICAL
Normalisation of sleep EEG (6 months)												
1 (Kwon 2013)	RCT	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/13 (15.4%)	3/16 (18.8%)	RR 0.82 (0.16 to 4.2)	34 fewer per 1000 (from 157 fewer to 600 more)	⊕OOO VERY LOW	IMPORTANT
EEG spike index - left (better indicated by lower values)												
1 (Kwon 2013)	RCT	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	13	16	-	MD 14.4 higher (0.55 to 28.25 higher)	⊕⊕OO LOW	IMPORTANT
EEG spike index - right (better indicated by lower values)												
1 (Kwon 2013)	RCT	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	13	16	-	MD 15.3 higher (4.57 to 26.03	⊕OOO VERY LOW	IMPORTANT

Quality assessment							Number of patients		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	OXC	No treat-ment	Relative (95% CI)	Absolute	Quality	Importance
										higher)		
Full scale intelligence quotient (6 months) (better indicated by higher values)												
1 (Kwon 2013)	RCT	serious[1]	no serious inconsistency	no serious indirectness	serious[4]	none	13	16	-	MD 13.8 lower (23.78 to 3.82 lower)	⊕⊕OO LOW	IMPORTANT

1 Serious risk of bias in the evidence contributing to the outcomes as per RoB 2
2 Confidence interval crosses both MIDs (0.8 and 1.25)
3 95% CI crosses 1 MID (+/-0.5 x control group SD for mean reduction in spike index - left = +/- 10)
4 95% CI crosses 1 MID (+/-0.5 x control group SD for mean difference in full-scale intelligence quotient - left = +/- 9.3)

Table 17: Clinical evidence profile. Comparison 5: clonazepam versus valporate

Quality assessment							Number of patients		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CZP	VPA	Relative (95% CI)	Absolute	Quality	Importance
Disappearance of RD on EEG (follow-up mean 4 weeks)												
1 (Mitsudome 1997)	RCT	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	15/20 (75%)	1/10 (10%)	RR 7.5 (1.15 to 48.98)	650 more per 1000 (from 15	⊕OOO VERY LOW	IMPORTANT

Quality assessment							Number of patients		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CZP	VPA	Relative (95% CI)	Absolute	Quality	Importance
										more to 1000 more)		

[1] *Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2*
[2] *Confidence interval crosses 1 MID (0.8 or 1.25)*

Table 18: Clinical evidence profile. Comparison 6: clonazepam versus carbamazepine

Quality assessment							Number of patients		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CZP	CBZ	Relative (95% CI)	Absolute	Quality	Importance
Disappearance of RD on EEG (follow-up mean 4 weeks)												
1 (Mitsudome 1997)	RCT	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	15/20 (75%)	0/10 (0%)	POR 18.17 (4.09 to 80.86)	750 more per 1000 (from 530 more to 970 more)	⊕⊕OO LOW	IMPORTANT

[1] *Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2*

Table 19: Clinical evidence profile. Comparison 7: valporate versus carbamazepine

Quality assessment							Number of patients		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	VPA	CBZ	Relative (95% CI)	Absolute	Quality	Importance
Disappearance of RD in EEG (follow-up mean 4 weeks)												
1 (Mitsudome 1997)	RCT	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/10 (10%)	0/10 (0%)	POR 7.39 (0.15 to 372.38)	100 more per 1000 (140 fewer to 340 more)	⊕OOO VERY LOW	IMPORTANT

[1] *Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2*
[2] *Confidence intervals cross both MIDs (0.8 and 1.25)*

Table 20: Clinical evidence profile. Comparison 8: sultiame versus placebo

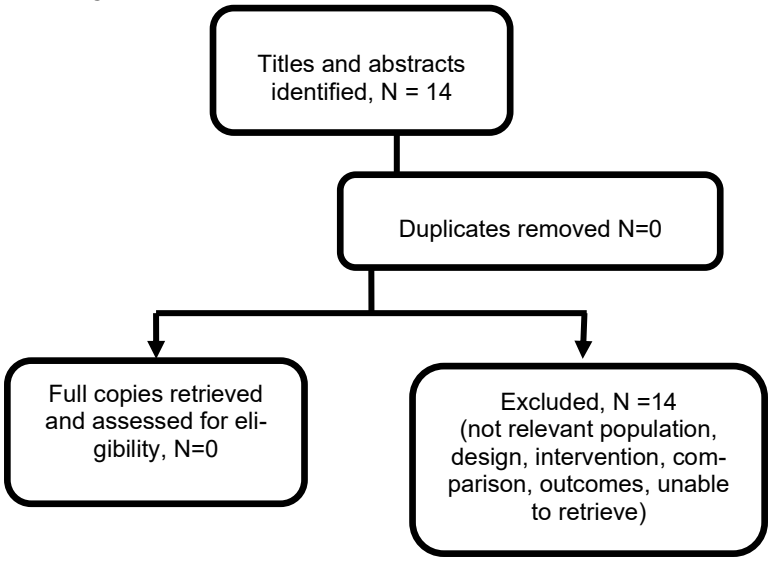
Quality assessment							Number of patients		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	STM	Placebo	Relative (95% CI)	Absolute	Qual-ity	Importance
Treatment failure (follow-up mean 6 months)												
1 (Rating 2000)	RCT	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	6/31 (19.4%)	25/35 (71.4%)	RR 0.27 (0.13 to 0.57)	521 fewer per 1000 (from 307 fewer to 621 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
EEG: specific pathology - Awake EEG (follow-up mean 6 months)												

Quality assessment							Number of patients		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	STM	Placebo	Relative (95% CI)	Absolute	Qual-ity	Importance
1 (Rating 2000)	RCT	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	10/25 (40%)	5/10 (50%)	RR 0.8 (0.37 to 1.75)	100 fewer per 1000 (from 315 fewer to 375 more)	⊕⊕OO LOW	IMPORTANT
EEG: normal - Awake EEG (follow-up mean 6 months)												
1 (Rating 2000)	RCT	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	11/25 (44%)	2/10 (20%)	RR 2.2 (0.59 to 8.2)	240 more per 1000 (from 82 fewer to 1000 more)	⊕⊕OO LOW	IMPORTANT
EEG: specific pathology - Sleep EEG (follow-up mean 6 months)												
1 (Rating 2000)	RCT	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	10/25 (40%)	6/10 (60%)	RR 0.67 (0.33 to 1.34)	198 fewer per 1000 (from 402 fewer to 204 more)	⊕⊕OO LOW	IMPORTANT
EEG: normal - Sleep EEG (follow-up mean 6 months)												
1 (Rating 2000)	RCT	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	10/25 (40%)	1/10 (10%)	RR 4 (0.59 to 27.29)	300 more per 1000 (from 41 fewer to 1000 more)	⊕⊕OO LOW	IMPORTANT

[1] *Confidence interval crosses both MIDs (0.8 and 1.25)*

Appendix G – Economic evidence study selection

Figure 3: Economic evidence study selection for review question: What antiseizure medications (monotherapy or add-on) are effective in the treatment of self-limited epilepsy with centrotemporal spikes? (2026 update)



Appendix H – Economic evidence tables

Economic evidence tables for review question: What antiseizure medications (monotherapy or add-on) are effective in the treatment of self-limited epilepsy with centrotemporal spikes?

No evidence was identified which was applicable to this review question.

Appendix I – Economic evidence profiles

Economic evidence profiles for review question: What antiseizure medications (monotherapy or add-on) are effective in the treatment of self-limited epilepsy with centrotemporal spikes?

No evidence was identified which was applicable to this review question.

Appendix J – Economic analysis

Economic evidence analysis for review question: What antiseizure medications (monotherapy or add-on) are effective in the treatment of self-limited epilepsy with centrotemporal spikes?

No economic analysis was conducted for this review question.

Appendix K – Excluded studies

Excluded clinical and economic studies for review question: What antiseizure medications (monotherapy or add-on) are effective in the treatment of self-limited epilepsy with centrotemporal spikes?

Clinical studies

Table 21: Excluded studies and reasons for their exclusion

Study	Reason for Exclusion
Akter, N., Rahman, M. M., Akhter, S., Fatema, K., A Randomized Controlled Trial of Phenobarbital and Levetiracetam in Childhood Epilepsy, Mymensingh Medical Journal: MMJ, 27, 776-784, 2018	Population does not meet the inclusion criteria: no specific reference to participants with CECTS
Ambrosetto, G., Tassinari, C. A., Antiepileptic drug treatment of benign childhood epilepsy with rolandic spikes: is it necessary?, Epilepsia, 31, 802-5, 1990	Study design does not meet inclusion criteria - retrospective case control study
Anderson, M., Choonara, I., A systematic review of safety monitoring and drug toxicity in published randomised controlled trials of antiepileptic drugs in children over a 10-year period, Archives of Disease in Childhood, 95, 731-738, 2010	Systematic review, no relevant data could be extracted for inclusion. References checked for inclusion
Andrade, R., García-Espinosa, A., Machado-Rojas, A., García-González, M. E., Trápaga-Quincoses, O., Morales-Chacón, L. M., A prospective, open, controlled and randomised study of clobazam versus carbamazepine in patients with frequent episodes of Rolandic epilepsy, Revista de neurologia, 49, 581-586, 2009	Publication not in English
Anonymous,, Clobazam has equivalent efficacy to carbamazepine and phenytoin as monotherapy for childhood epilepsy. Canadian Study Group for Childhood Epilepsy, Epilepsia, 39, 952-9, 1998	Population do not meet the inclusion criteria - no specific reference to participants with CECTS
Arya, R., Giridharan, N., Anand, V., Garg, S. K., Clobazam monotherapy for focal or generalized seizures, Cochrane Database of Systematic Reviews, 2018	Systematic review, relevant studies which meet the protocol inclusion criteria are already included
Arya, R., Glauser, T. A., Pharmacotherapy of focal epilepsy in children: A systematic review of approved agents, CNS Drugs, 27, 273-286, 2013	Systematic review. No relevant data could be extracted for inclusion. References checked for inclusion
Asadi-Pooya, A. A., Forouzesh, M., Eidi, H., Mirzaghafour, S. E., Levetiracetam versus carbamazepine in treatment of rolandic epilepsy, Epilepsy and Behavior, 94, 1-8, 2019	Systematic review, no relevant data could be extracted for inclusion. References checked for inclusion
Ay, Y., Gokben, S., Serdaroglu, G., Polat, M., Tosun, A., Tekgul, H., Solak, U., Kesikci, H., Neuropsychologic Impairment in Children With Rolandic Epilepsy, Pediatric Neurology, 41, 359-363, 2009	Study design does not meet the inclusion criteria - prospective case control study
Banu, S. H., Jahan, M., Koli, U. K., Ferdousi, S., Khan, N. Z., Neville, B., Side effects of phenobarbital and carbamazepine in childhood epilepsy: Randomised controlled trial, British Medical Jour-	Population does not meet the inclusion criteria: No specific reference to participants with CECTS

Study	Reason for Exclusion
nal, 334, 1207-1210, 2007	
Barik, K. L., Paul, U. K., Bhattacharyya, A. K., Adhikary, A., Agarwal, G., Rana, K. S., New onset paediatric epilepsy in 1-5 years age group children--approach to management in a tertiary care centre with newer anti-epileptic levetiracetam, Journal of the Indian Medical Association, 112, 100-2, 2014	Population does not meet the inclusion criteria: no specific reference to participants with CECTS
Basnec, A., Skarpa, D., BarisiÄ‡, N., Jurin, M., MuciÄ-PuciÄ, B., The risk of second seizure in children with benign childhood epilepsy with centrotemporal spikes without treatment--a prospective study, Acta medica Croatica, 59, 59â□□62, 2005	Publication not in English
Bast, T., Völp, A., Wolf, C., Rating, D., The influence of sulthiame on EEG in children with benign childhood epilepsy with centrotemporal spikes (BECTS), Epilepsia, 44, 215â□□220, 2003	Secondary publication from the included study, Rating 2000. The paper does not report any additional, relevant outcomes
Bawden, H. N., Camfield, C. S., Camfield, P. R., Cunningham, C., Darwish, H., Dooley, J. M., Gordon, K., Ronen, G., Stewart, J., van Mastrigt, R., The cognitive and behavioural effects of clobazam and standard monotherapy are comparable. Canadian Study Group for Childhood Epilepsy, Epilepsy Research, 33, 133-43, 1999	Population does not meet the inclusion criteria: No specific reference to participants with CECTS
Berg, I., Butler, A., Ellis, M., Foster, J., Psychiatric aspects of epilepsy in childhood treated with carbamazepine phenytoin or sodium valproate: A random trial, Developmental Medicine and Child Neurology, 35, 149-157, 1993	Population do not meet the inclusion criteria: No specific reference to participants with CECTS
Bonfert, M., Armbruster, S., Bastian, B., Heinen, F., Efficacy of levetiracetam in the treatment of children with BECTS: a prospective, open-label pilot trial prior to a controlled, randomised, double-blind German multicentre study (HEAD study), Epilepsia, 47 Suppl 3, 133, Abstract no: p510, 2006	Conference abstract
Borggraefe, I., Bonfert, M., Bast, T., Neubauer, B. A., Schotten, K. J., Massmann, K., Noachtar, S., Tuxhorn, I., May, T. W., Heinen, F., A double-blinded, randomized, head-to-head trial of levetiracetam vs. sulthiame in benign epilepsy with centrotemporal spikes, Epilepsy Currents, 1), 67, 2013	Conference abstract
Borggraefe, I., Bonfert, M., Gerstl, L., Heinen, F., Neubauer, B., A double-blinded, randomized evaluation of neuropsychological and behavioral changes in children with benign epilepsy with centrotemporal spikes treated either with levetiracetam or sulthiame, Epilepsy Currents, 1), 278, 2015	Conference abstract
Borggrafe, I., Bonfert, M., Bast, T., Neubauer, B. A., Schotten, K. J., Masmann, K., Noachtar, S., Tuxhorn, I., May, T. W., Heinen, F., A double-blinded, randomized, head-to-head trial of levetiracetam versus sulthiame in benign epilepsy with centrotemporal spikes, Neuropediatrics. Con-	Conference abstract

Study	Reason for Exclusion
ference: 39th Annual Meeting of the Society of Neuropediatrics. Innsbruck Austria. Conference Publication:, 44, 2013	
Bourgeois, B., Brown, L. W., Pellock, J. M., Buroker, M., Greiner, M., Garofalo, E. A., Schimschock, J. R., Griesemer, D., Bebin, M. E., Murphy, J. V., Gabapentin (Neurontin) monotherapy in children with benign childhood epilepsy with centrotemporal spikes (BECTS): a 36-week, double-blind, placebo-controlled study, Epilepsia, 39 Suppl 6, 163, 1998	Conference abstract
Braathen, G., Andersson, T., Gylje, H., Melander, H., Naglo, A. S., Noren, L., Persson, A., Rane, A., Sjors, K., Theorell, K., Wigertz, A., Comparison between one and three years of treatment in uncomplicated childhood epilepsy: A prospective study. I. Outcome in different seizure types, Epilepsia, 37, 822-832, 1996	Intervention does not meet inclusion criteria: The study compares 1 to 3 years of treatment, not different treatment types
Callenbach, P. M. C., Bouma, P. A. D., Geerts, A. T., Arts, W. F. M., Stroink, H., Peeters, E. A. J., Van Donselaar, C. A., Peters, A. C. B., Brouwer, O. F., Long term outcome of benign childhood epilepsy with centrotemporal spikes: Dutch Study of Epilepsy in Childhood, Seizure, 19, 501-506, 2010	Study design does not meet the inclusion criteria - prospective cohort study
Camfield, P., Booth, F., Buckley, D., Camfield, C., Darwish, H., Dooley, J., Farrell, K., Gordon, K., Hwang, P., Langevin, P., Larbrisseau, A., Lowry, N., Meek, D., Munn, R., Reggin, J., Ronen, G., Sinclair, B., Tibbles, J., Whiting, S., Wilfong, A., Yager, J., Stewart, J., Clobazam has equivalent efficacy to carbamazepine and phenytoin as monotherapy for childhood epilepsy, Epilepsia, 39, 952-959, 1998	Population does not meet the inclusion criteria: No specific reference to participants with CECTS
Chen, Y. J., Kang, W. M., So, W. C. M., Comparison of antiepileptic drugs on cognitive function in newly diagnosed epileptic children: A psychometric and neurophysiological study, Epilepsia, 37, 81-86, 1996	Population does not meet the inclusion criteria: No specific reference to participants with CECTS
Cheng, Wenwen, Yang, Yan, Chen, Ying et al. (2022) Anti-Seizure Medication Treatment of Benign Childhood Epilepsy With Centrotemporal Spikes: A Systematic Review and Meta-analysis. Frontiers in pharmacology 13: 821639	Systematic review used as a source of primary studies *Systematic review. No relevant data could be extracted for inclusion. References checked for inclusion*
Clemens, B., Menes, A., Piros, P., Bessenyei, M., Altmann, A., Jerney, J., Kollar, K., Rosdy, B., Rozsavolgyi, M., Steinecker, K., Hollody, K., Quantitative EEG effects of carbamazepine, oxcarbazepine, valproate, lamotrigine, and possible clinical relevance of the findings, Epilepsy Research, 70, 190-9, 2006	Study design does not meet the inclusion criteria - non-randomized, cohort screening study
Connock, M., Frew, E., Evans, B. W., Bryan, S., Cummins, C., Fry-Smith, A., Li Wan Po, A., Sandercock, J., The clinical effectiveness and cost-effectiveness of newer drugs for children with epilepsy. A systematic review, Health Tech-	Systematic review, no relevant data could be extracted for inclusion. References checked for inclusion

Study	Reason for Exclusion
nology Assessment, 10, iii-118, 2006	
Coppola, G., Franzoni, E., Verrotti, A., Garane, C., Sarajlija, J., Operto, F., Pascotto, A., Levetiracetam or oxcarbazepine as monotherapy in newly diagnosed benign rolandic seizures in children: an open-label, parallel group study, Epilepsia, 47 Suppl 3, 179â□□180, 2006	Conference abstract
Cross, J. H., Auvin, S., Patten, A., Giorgi, L., Safety and tolerability of zonisamide in paediatric patients with epilepsy, European Journal of Paediatric Neurology, 18, 747-758, 2014	Systematic review, no data relevant could be extracted for inclusion. References checked for inclusion
Ctri,, Study of effect of treatment versus no treatment on seizures, psychological, behavioral and EEG parameters in children with BECTS type of epilepsy, Http://www.who.int/trialsearch/trial2.aspx? Trialid=ctri/2018/02/012248, 2018	Trial registration
De Goede, C. G., Gupta, R., Antiepileptic drugs versus no treatment or placebo for children with benign epilepsy with centro temporal spikes, Cochrane Database of Systematic Reviews, (4) (no pagination), 2007	Protocol
De Negri, M., Baglietto, M. G., Gaggero, R., Benzodiazepine (BDZ) treatment of benign childhood epilepsy with centrotemporal spikes (BECCT), Brain & Development, 19, 506, 1997	Letter to the editor
De Paola, L., The not so benign idiopathic focal epilepsies of childhood: A second look on the benign childhood epilepsy with centrotemporal spikes (BECTS), Arquivos de Neuro-Psiquiatria, 61, 59-64, 2003	Narrative review
De Silva, M., MacArdle, B., McGowan, M., Hughes, E., Stewart, J., Neville, B. G. R., Johnson, A. L., Reynolds, E. H., Randomised comparative monotherapy trial of phenobarbitone, phenytoin, carbamazepine, or sodium valproate for newly diagnosed childhood epilepsy, Lancet, 347, 709-713, 1996	Population does not meet the inclusion criteria: No specific reference to participants with CECTS
Deonna, T., Roulet-Perez, E., Cronel-Ohayon, S., Mayor-Dubois, C., Correspondence on "deterioration in cognitive function in children with benign epilepsy of childhood with central temporal spikes treated with sulthiame", Journal of Child Neurology, 25, 127-8, 2010	Letter to the editor
Dulac, O., Lamotrigine in the treatment of childhood epilepsy, Bollettino - Lega Italiana contro l'Epilessia, 37-38, 1994	Population do not meet the inclusion criteria - no specific reference to participants with CECTS
Euctr, D. E., HEAD-TO-HEAD evaluation of the antiepileptic drugs Levetiracetam (LEV) vs. Sulthiame (STM) in a German multi-centre, double-blind controlled trial in children with benign epilepsy with centro-temporal spikes - HEAD-STUDIE, Http://www.who.int/trialsearch/trial2.aspx? Trialid=euctr2005-004468-22-de, 2006	Trial registration
Euctr, G. B., Sleep and learning in children with a	Trial registration

Study	Reason for Exclusion
benign focal epilepsy of childhood, Http://www.who.int/trialsearch/trial2.aspx? Trial-id=euctr2011-001571-39-gb, 2011	
Eun, S. H., Eun, B. L., Lee, J. S., Hwang, Y. S., Kim, K. J., Lee, Y. M., Lee, I. G., Lee, M., Ko, T. S., Kim, J. T., Eom, S., Kim, H. D., Effects of lamotrigine on cognition and behavior compared to carbamazepine as monotherapy for children with partial epilepsy, Brain and Development, 34, 818-823, 2012	Population do not meet the inclusion criteria - no specific reference to participants with CECTS
Eun, S. H., Kim, H. D., Eun, B. L., Lee, I. K., Chung, H. J., Kim, J. S., Kang, H. C., Lee, Y. M., Suh, E. S., Kim, D. W., Eom, S., Lee, J. S., Moon, H. K., Comparative trial of low- and high-dose zonisamide as monotherapy for childhood epilepsy, Seizure, 20, 558-563, 2011	Outcome data does not meet the inclusion criteria - despite reference to participants with CECTS no data are reported separately for these participants
Eun, S. H., Kim, H. D., Lee, I. K., Chung, H. J., Eun, B. L., Lee, J. S., Kim, J. S., Kang, H. C., Suh, E. S., Kim, D. W., Eom, S., Moon, H. K., A multicenter comparative trial of low and high dose zonisamide in children with newly diagnosed epilepsy as monotherapy, Epilepsia, 4), 147, 2010	Conference abstract
Eun, S., Kim, H., Lee, I., Chung, H., Eun, B., Lee, J., Kim, J., Kang, H., Suh, E., Kim, D., Eom, S., Moon, H., A multi-center comparative trial of low and highdose zonisamide in children with newly diagnosed epilepsy as monotherapy, Epilepsia, 11), 244, 2009	Conference abstract
Feng, Jun, Zhang, Liya, Tang, Jihong et al. (2024) Clinical Analysis of Lacosamide Monotherapy in the Treatment of Self-Limited Epilepsy with Centrotemporal Spikes. Neuropsychiatric disease and treatment 20: 459-467	Study design not relevant to this review protocol *Retrospective cohort study*
Forsythe, I., Butler, R., Berg, I., McGuire, R., Cognitive impairment in new cases of epilepsy randomly associated to carbamazepine, phenytoin and sodium valproate, Developmental Medicine and Child Neurology, 33, 524-534, 1991	Population do not meet the inclusion criteria - no specific reference to participants with CECTS
Freydkova, N., Karlov, V., Topamax monotherapy in cases of children's and adolescent's focal epilepsy, Epilepsia, 4), 132, 2009	Conference abstract
Geng, H., Wang, C., Efficacy and safety of oxcarbazepine in the treatment of children with epilepsy: A metaanalysis of randomized controlled trials, Neuropsychiatric Disease and Treatment, 13, 685-695, 2017	Systematic review, no relevant data could be extracted for inclusion. References checked for inclusion
Gerstl, L., Willimsky, E., Remi, C., Noachtar, S., Borggrafe, I., Tacke, M., A Systematic Review of Seizure-Freedom Rates in Patients With Benign Epilepsy of Childhood With Centrotemporal Spikes Receiving Antiepileptic Drugs, Clinical neuropharmacology, 2021	Systematic review. All studies already included in NGA review with the exception of Andrade (2009) which is not available in English.
Gkampeta, A., Fidani, L., Zafeiriou, D., Pavlou, E., Benign epilepsy with centrotemporal spikes: Relationship between type of seizures and response to medication in a Greek population, Journal of Neurosciences in Rural Practice, 6,	Study design does not meet the inclusion criteria - participants were not randomised but grouped according to seizure type

Study	Reason for Exclusion
545-548, 2015	
Glauser, T. A., Ayala, R., Elterman, R. D., Mitchell, W. G., Van Orman, C. B., Gauer, L. J., Lu, Z., Double-blind placebo-controlled trial of adjunctive levetiracetam in pediatric partial seizures, Neurology, 66, 1654-1660, 2006	Population do not meet the inclusion criteria - no specific reference to participants with CECTS
Glauser, T., Ben-Menachem, E., Bourgeois, B., Cnaan, A., Guerreiro, C., Kalviainen, R., Mattson, R., French, J. A., Perucca, E., Tomson, T., Updated ILAE evidence review of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes, Epilepsia, 54, 551-563, 2013	Systematic review, no relevant data could be extracted for inclusion. References checked for inclusion
Haigh, D., Forsythe, W. I., The treatment of childhood epilepsy with sodium valproate, Developmental Medicine & Child Neurology, 17, 743-8, 1975	Study design does not meet the inclusion criteria - non-randomised, case series
Halma, E., De Louw, A. J. A., Klinkenberg, S., Aldenkamp, A. P., Ijff, D. M., Majoie, M., Behavioral side-effects of levetiracetam in children with epilepsy: A systematic review, Seizure, 23, 685-691, 2014	Systematic review, no relevant data could be extracted for inclusion. References checked for inclusion
Kanemura, H., Sano, F., Ohyama, T., Sugita, K., Aihara, M., Effect of Levetiracetam Monotherapy in Nonlesional Focal Childhood Epilepsy, Neuropediatrics, 49, 135-141, 2018	Study design does not meet the inclusion criteria - retrospective review of data
Kang, H. C., Eun, B. L., Lee, C. W., Moon, H. K., Kim, J. S., Kim, D. W., Lee, J. S., Chae, K. Y., Cha, B. H., Suh, E. S., et al.,, A multicenter, randomized, open-labeled, clinical study to evaluate the effect on cognitive and behavioral function of topiramate compared with carbamazepine as monotherapy in children with benign rolandic epilepsy, Epilepsia, 47, 138, Abstract no: 2.057, 2006	Conference abstract
Kramer, U., Shahar, E., Zelnik, N., Lerman-Sagie, T., Watemberg, N., Nevo, Y., Ben-Zeev, B., Carbamazepine versus sulthiame in treating benign childhood epilepsy with centrotemporal spikes, Journal of Child Neurology, 17, 914-6, 2002	Study design does not meet the inclusion criteria - non-randomised, case series
Kwok, S. C., Paediatric epilepsy website, Journal of Paediatrics and Child Health, 54, 1268, 2018	Commentary paper
Lagae, L., Buyse, G., Ceulemans, B., Clinical experience with levetiracetam in childhood epilepsy: an add-on and mono-therapy trial, Seizure, 14, 66-71, 2005	Study design does not meet the inclusion criteria - on-randomised cohort study Additionally, the population do not meet the inclusion criteria: No specific reference to participants with CECTS
Lagae, L., Meshram, C., Giorgi, L., Patten, A., Effects of adjunctive zonisamide treatment on weight and body mass index in children with partial epilepsy, Acta Neurologica Scandinavica, 131, 341-346, 2015	Outcomes do not meet the inclusion criteria - data on BMI and weight only. Primary trial checked for inclusion but is not relevant as the population does not meet the inclusion criteria - No specific reference to participants with CECTS
Lenz,R.A., Elterman,R.D., Robieson,W.Z., Vigna,N.V., Saltarelli,M.D., Divalproex Sodium in Children with Partial Seizures: 12-Month Safety	Population do not meet the inclusion criteria - no specific reference to participants with CECTS

Study	Reason for Exclusion
Study, Pediatric Neurology, 41, 101-110, 2009	
Lim, K., Kim, H. D., Low-dose topiramate compared with carbamazepine in treating benign rolandic epilepsy, Epilepsia, 45, 322â□□323, 2004	Conference abstract
Liu, C., Song, M., Wang, J., Nightly oral administration of topiramate for benign childhood epilepsy with centrotemporal spikes, Child's Nervous System, 32, 839-843, 2016	Intervention does not meet the inclusion criteria - compares once nightly with twice daily Topiramate
Liu, M. J., Su, X. J., Md, X. S., Wu, G. F., Zhang, Y. Q., Gao, L., Wang, W., Liao, J. X., Wang, H., Mai, J. N., Gao, J. Y., Shu, X. M., Huang, S. P., Zhang, L., Zou, L. P., Clinical features of benign epilepsy of childhood with centrotemporal spikes in chinese children, Medicine, 96, e5623, 2017	Study design does not meet the inclusion criteria - retrospective review of current practice in Study design does not meet the inclusion criteria - prospective cohort
Liu, Y., Wang, Y., Li, X. et al. (2024) Efficacy and safety of levetiracetam vs. oxcarbazepine in the treatment of children with epilepsy: a systematic review and meta-analysis. Frontiers in Pediatrics 12: 1336744	Systematic review used as a source of primary studies *Systematic review. No relevant data could be extracted for inclusion. References checked for inclusion*
Maheshwari, M. C., Sodium valproate in the treatment of childhood epilepsies, Indian Pediatrics, 21, 439-46, 1984	Narrative review
Messenheimer, J., Efficacy and safety of lamotrigine in pediatric patients, Journal of Child Neurology, 17, 2S34-2S42, 2002	Narrative review
Messenheimer,J.A., Giorgi,L., Risner,M.E., The tolerability of lamotrigine in children, Drug Safety, 22, 303-312, 2000	Narrative review
Milburn-McNulty, P., Powell, G., Sills, G. J., Marson, A. G., Sulthiame monotherapy for epilepsy, Cochrane Database of Systematic Reviews, CD010062, 2014	Systematic review, no relevant data could be extracted for inclusion. References checked for inclusion
Mitsudome, A., Ohu, M., Yasumoto, S., Ogawa, A., Rhythmic slow activity in benign childhood epilepsy with centrotemporal spikes, Clinical Electroencephalography, 28, 44-8, 1997	Study design does not meet the inclusion criteria - prospective cohort of four participants
Miura, H., Minagawa, K., Kaneko, T., Sudo, Y., Sodium valproate as a single drug in the treatment of childhood epilepsy: A prospective study of plasma levels and seizure control, Brain and Development, 3, 196, 1981	Conference abstract
Miura, H., Minagawa, K., Kaneko, T., Sudo, Y., Carbamazepine as a single drug in the treatment of childhood epilepsy: A prospective study of plasma levels and seizure control, Brain and Development, 2, 272, 1980	Conference abstract
Morris, G. L., Gabapentin, Epilepsia, 40, S63-S70, 1999	Narrative review
Nct,, HEAD-Study Optimizing the Treatment of Children With BECTS, Https://clinicaltrials.gov/show/nct00471744, 2007	Trial registration
Nct,, Electroclinical Effect of Diazepam and Steroid in Patients With Benign Childhood Epilepsy With Centrotemporal Spikes,	Trial registration.

Study	Reason for Exclusion
Https://clinicaltrials.gov/show/nct03490487, 2018	
O'Donohoe, N. V., Use of antiepileptic drugs in childhood epilepsy, Archives of Disease in Childhood, 66, 1173-1175, 1991	Narrative review
Ormrod, D., McClellan, K., Topiramate: A review of its use in childhood epilepsy, Paediatric Drugs, 3, 293-319, 2001	Narrative review
Rai, A., Aggarwal, A., Mittal, H., Sharma, S., Comparative efficacy and safety of intravenous valproate and phenytoin in children, Pediatric Neurology, 45, 300-304, 2011	Population do not meet the inclusion criteria - no specific reference to participants with CECTS
Rating, D., Wolf, Ch, Sulthiame vs placebo in the treatment of benign epilepsy with centrotemporal spikes ("Rolandic" Epilepsy), Epilepsia, 40 Suppl 2, 163, 1999	Conference abstract
Rosati, A., De Masi, S., Guerrini, R., Antiepileptic Drug Treatment in Children with Epilepsy, CNS Drugs, 29, 847-863, 2015	Narrative review
Rosati, A., Ilvento, L., Lucenteforte, E., Pugi, A., Crescioli, G., McGreevy, K. S., Virgili, G., Mugelli, A., De Masi, S., Guerrini, R., Comparative efficacy of antiepileptic drugs in children and adolescents: A network meta-analysis, Epilepsia, 59, 297-314, 2018	Systematic review, no relevant data could be extracted for inclusion. References checked for inclusion
Rufo-Campos, M., Casas-Fernandez, C., Martinez-Bermejo, A., Long-term use of oxcarbazepine oral suspension in childhood epilepsy: Open-label study, Journal of Child Neurology, 21, 480-485, 2006	Population do not meet the inclusion criteria - no specific reference to participants with CECTS
Sankar, R., Update on the pharmacologic management of common pediatric epilepsy syndromes, No To Hattatsu, 48 (Supplement 1), S210, 2016	Publication not in English
Schlumberger, E., Chavez, F., Palacios, L., Rey, E., Pajot, N., Dulac, O., Lamotrigine in treatment of 120 children with epilepsy, Epilepsia, 35, 359-67, 1994	Population do not meet the inclusion criteria - no specific reference to participants with CECTS
Tacke, M., EEG changes in rolandic epilepsy under treatment with Levetiracetam and Sulthiame, European Journal of Paediatric Neurology, 21 (Supplement 1), e97, 2017	Conference abstract
Tacke, M., Gerstl, L., Heinen, F., Heukaeufer, I., Bonfert, M., Bast, T., Cornell, S., Neubauer, B. A., Borggraefe, I., Effect of anticonvulsive treatment on neuropsychological performance in children with BECTS, European journal of paediatric neurology: EJPN, 20, 874-879, 2016	Outcome data not extractable for analysis
Tacke, M., Rupp, N., Gerstl, L., Heinen, F., Vill, K., Bonfert, M., Neubauer, B. A., Bast, T., Borggraefe, I., Baumeister, F. A. M., Baethmann, M., Schreiber-Gollwitzer, B., Bentele, K., Blank, C., Held, J., Blank, H. M., Liebrich, K., Bode, H., Braun, J., Bosch, F., Wagner, R., Brandl, U., Wetzel, K., Brockmann, K., Schlockwerder, C., Dahlem, P., Baudler, I., Ernst, J. P., Mayer, H., Feldmann, E., Pattber-Wolff, A., Fiedler, A.,	Outcomes do not meet the inclusion criteria - secondary publication from the included study, Broggraefe 2013

Study	Reason for Exclusion
Sonnleitner, S., Gerigk, M., Hess, S., Feiereis, T., Hikel, C., Hoffmann, H. G., Rickeshenrich, A., Kieslich, M., Dewitz, R., Baz Bartels, M., Klepper, J., Kleuker, S., Kluger, G., Kirsch, A., Koch, H., Meerpohl, U., Koch, W., Korinthenberg, R., Steh-le-Renner, B., Krois, I., Wegener, A., Kuhne, H., Weiss, C., Kurlemann, G., Elkemann, U., Mandl, M., Friedl, A., Mause, U., Muller, M., Navratil, P., Iken, U., Opp, J., Walter, J., Penzien, J., Prietsch, V., Siegrist, B., Quattlander, A., Rating, D., Reuner, G., Schara, U., Shamdeen, M. G., Struchholz, H., prinz, A., Wendker-Magrabi, H., Stephani, U., Muhle, H., Carlsson, G., Strassburg, H. M., Ottensmeier, H., Topke, B., Tatsek, K., Trollmann, R., Poida-Herzing, E., Tuschen-Hofstatter, E., Menschig, M., Waltz, S., Pickartz, A., Weber, G., Gehnen, T., Wien, F. U., Ante-mann, J., Wolff, M., Serra, E., Polster, T., Freitag, H., Sonmez, O., Rheinhardt, K., Traus, M., chroder, A., Hoovey, S., Navratil, C., Benign epi-lepsy with centrotemporal spikes: Correlating spike frequency and neuropsychology, Acta Neu-rologica Scandinavica, 138, 475-481, 2018	
Takahashi, K., Saito, M., Kyo, K., Gomibuchi, K., Niijima, S., Tada, H., Honda, T., Sato, Y., Takahashi, H., Ohtsuka, C., The effects of clonazepam on rolandic discharge of benign epi-lepsy of children with centro-temporal EEG foci, Japanese Journal of Psychiatry & Neurology, 45, 468-70, 1991	Study design does not meet the inclusion crite-ria - non-randomised follow up study
Tan, H. J., Singh, J., Gupta, R., de Goede, C., Comparison of antiepileptic drugs, no treatment, or placebo for children with benign epilepsy with centro temporal spikes, Cochrane Database of Systematic Reviews, 2014 (9) (no pagination), 2014	Systematic review, relevant studies which meet the protocol inclusion criteria are already in-cluded in the NGA review
Trudeau, V. L., Kilgore, M. B., Poulter, C. J., DuMetz, M. K., Gillem, C. H., Hes, M. S., Koto, E. M., Garofalo, E. A., A multicenter, open-label ex-tension study of gabapentin (Neurontin) mono-therapy in pediatric patients with benign epilepsy with centrotemporal spikes (BECTS), Epilepsia, 37 Suppl 5, 111, 1996	Conference abstract
Van Sweden, B., VPA syrup in childhood epilep-sy. Results of an international clinical multicentre trial, Acta Neurologica Belgica, 88, 152-62, 1988	Population do not meet the inclusion criteria - no specific reference to participants with CECTS
Verdru, P., Epilepsy in children: The evidence for new antiepileptic drugs, Acta Neurologica Scan-dinavica, 112, 17-20, 2005	Narrative review
Verity, C. M., Hosking, G., Easter, D. J., A multi-centre comparative trial of sodium valproate and carbamazepine in paediatric epilepsy, ESSAI COMPARATIF DU VALPROATE DE SODIUM ET DE LA CARBAMAZEPINE SUR L'EPILEPSIE DE L'ENFANT, DANS PLUSIEURS CENTRES, De-velopmental Medicine and Child Neurology, 37, 97-108, 1995	Population do not meet the inclusion criteria - no specific reference to participants with CECTS
Verrotti, A., D'Egidio, C., Agostinelli, S., Parisi, P.,	Study design does not meet the inclusion crite-

Study	Reason for Exclusion
Chiarelli, F., Coppola, G., Cognitive and linguistic abnormalities in benign childhood epilepsy with centrotemporal spikes, Acta Paediatrica, International Journal of Paediatrics, 100, 768-772, 2011	ria - non-randomised follow up study
Wang, Y. Y., Wang, M. G., Yao, D., Huang, X. X., Zhang, T., Deng, X., Comparison of impact on seizure frequency and epileptiform discharges of children with epilepsy from topiramate and phenobarbital, European Review for Medical and Pharmacological Sciences, 20, 993-997, 2016	Population do not meet the inclusion criteria - no specific reference to participants with CECTS
Weijenberg, A., Brouwer, O. F., Callenbach, P. M. C., Levetiracetam Monotherapy in Children with Epilepsy: A Systematic Review, CNS Drugs, 29, 371-382, 2015	Systematic review, no relevant data could be extracted for inclusion. References checked for inclusion
Weijenberg, A., Offringa, M., Brouwer, O. F., Callenbach, P. M. C., RCTs with new antiepileptic drugs in children: A systematic review of monotherapy studies and their methodology, Epilepsy Research, 91, 1-9, 2010	Systematic review, no relevant data could be extracted for inclusion. References checked for inclusion
Wheless, J. W., Use of topiramate in childhood generalized seizure disorders, Journal of Child Neurology, 15, S7-S13, 2000	Narrative review
Wheless, J. W., Neto, W., Wang, S., Topiramate, carbamazepine, and valproate monotherapy: Double-blind comparison in children with newly diagnosed epilepsy, Journal of Child Neurology, 19, 135-141, 2004	Population do not meet the inclusion criteria - no specific reference to participants with CECTS
Yamawaki, H., Seki, T., Suzuki, N., Single-drug therapy with valproic acid in childhood epilepsy, Folia Psychiatrica et Neurologica Japonica, 36, 320, 1982	Study design does not meet the inclusion criteria - non-randomised case series
Yasuhara, A., Matsuoka, O., Tamai, H., Suzuki, Y., Imai, K., Woo, M., Hattori, H., Mimaki, T., Nagai, T., Sugimoto, T., Murata, R., Okada, S., Prospective study of benign childhood epilepsy with centrotemporal spikes: Preliminary study, Japanese Journal of Psychiatry and Neurology, 48, 375-377, 1994	Study design does not meet the inclusion criteria - non-randomised cohort
Yi, Z. M., Wen, C., Cai, T., Xu, L., Zhong, X. L., Zhan, S. Y., Zhai, S. D., Levetiracetam for epilepsy: An evidence map of efficacy, safety and economic profiles, Neuropsychiatric Disease and Treatment, 15, 1-19, 2019	Systematic review of systematic reviews and trials. No relevant data could be extracted for inclusion. References checked for inclusion
Zhou, S., Zhan, Q., Wu, X., Effect of levetiracetam on cognitive function and clonic seizure frequency in children with epilepsy, Current molecular medicine., 29, 2019	Population do not meet the inclusion criteria - no specific reference to participants with CECTS

Economic studies

No economic evidence was identified for this review.

Appendix L – Research recommendations

Research recommendations for review question: What antiseizure medications (monotherapy or add-on) are effective in the treatment of self-limited epilepsy with centrotemporal spikes?

No research recommendations were made for this review question.