Health Technology Briefing
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Sulthiame for treating self-limiting epilepsy with centrotemporal spikes in children

Company/Developer	Desitin Arzneimittel

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 39057	NICE ID: Not available	UKPS ID: 674937

Licensing and Market Availability Plans

Clinical trials completed.

Summary

Sulthiame is in development for the treatment of self-limiting epilepsy with centrotemporal spikes in children. A self-limiting epilepsy with centrotemporal spikes is defined as an age-dependent epilepsy, with a typical onset at 5–8 years that usually subsides by the teenage years. The main symptom of the condition is seizures lasting between 1 – 3 mins. It is a hereditary health condition. Generally, epilepsy cannot be controlled by current antiseizure medications in at least 30% of patients so new treatments are needed.

Sulthiame is a medicinal product that works by inhibiting an enzyme called carbonic anhydrase in glial (brain) cells. This changes the environment around the cells to reduce electrical activity in the brain/ nerve cells to reduce/ prevent seizures. If licensed, sulthiame may provide a new treatment option for self-limiting epilepsy with centrotemporal spikes in children.

Proposed Indication

Treatment of self-limiting epilepsy with centrotemporal spikes (SeLECTS) in children.[1,2]

Technology

Description

Sulthiame (Ospolot) is a carbonic anhydrase inhibitor (CAI).[3] Carbonic anhydrases (CAs) are a group of ubiquitously expressed metalloenzymes that catalyse the reversible hydration/dehydration of carbon dioxide/bicarbonate. CAs represent molecular targets for epilepsy and the interference with their activity, through specific inhibitors (CAIs), has an anticonvulsive outcome.[4] CAIs are, therefore, a type of medication used to manage and treat epilepsy, among other diseases.[5] Sulthiame (STM), therefore, inhibits the enzyme carbonic anhydrase in glial cells which increases carbon dioxide concentrations leading to acidification of the extracellular space; this results in a reduction in inward currents associated with N-methyl-D-aspartate calcium receptors and causes depression of intrinsic neuronal excitability.[6]

STM is currently in development for the treatment of self-limiting epilepsy with centrotemporal spikes in children. In the clinical trial (PMID: 23642492), participants received 2 mg/kg body weight initial dose of STM, followed by a weekly increase of 2 mg/kg body weight.[1] In another clinical trial (PMID: 11051123), participants received 5 mg/kg/day of STM.[2]

Key Innovation

In at least 30% of patients, epilepsy cannot be controlled by current antiseizure medications.[7] STM is an antiseizure medication with a mechanism of action primarily involving inhibitory effects on CAs and reduces the frequency of action potentials and epileptiform bursts.[6,8] Treatment with STM aims to achieve complete seizure remission or reduce frequency/ severity of seizures in patients.[6] When compared with a standard of care, STM presented fewer adverse events.[1] If licensed, STM may provide a new treatment option for self-limiting epilepsy with centrotemporal spikes in children.

Regulatory & Development Status

STM does not currently have Marketing Authorisation in the UK for any indication.

STM is also currently in phase II/III development for Obstructive Sleep Apnea.[9]

Patient Group

Disease Area and Clinical Need

Epilepsy is a common condition that affects the brain and causes frequent seizures. Seizures are bursts of electrical activity in the brain that temporarily affect how it works. They can cause a wide range of symptoms.[10] SeLECTS is also known as benign rolandic epilepsy (BRE) or benign epilepsy with centrotemporal spikes (BECTS).[11,12] It is defined as an age-dependent epilepsy, with a typical onset at 5–8 years.[13] The main symptom of epilepsy is repeated seizures.[14] In SeLECTS, the seizures are usually infrequent, brief and lasting between 1 – 3 mins. Other symptoms of SeLECTS include; unilateral facial sensorimotor symptoms, oropharyngolaryngeal manifestations, speech arrest, and hypersalivation.[11] Genetic predisposition with complex modes of inheritance has been suggested in SeLECTS, as different family studies indicated that centrotemporal spikes may be transmitted as an autosomal dominant trait

with age-dependent penetrance and multifactorial inheritance.[11] As SeLECTS is an age-related epilepsy syndrome which subsides by early teenage years and the seizures can be infrequent and confined to sleep with limited impact on the child's well-being, the main decision is whether to treat with antiseizure medications due to potential adverse events.[15]

SeLECTS is the most common focal epilepsy syndrome of childhood, accounting for 15–20% of all childhood epilepsies.[13] Patients with epilepsy carry a risk of premature death which is on average two to three times higher than in the general population. The risk of death is not homogenously distributed over all ages, aetiologies, and epilepsy syndromes.[16] In England (2022-23) there were 50,352 finished consultant episodes (FCEs) and 35,071 admissions for epilepsy (ICD-10 code G40), which resulted in 4,368 day cases and 124,071 FCE bed days.[17]

Recommended Treatment Options
There are currently no National Institute for Health and Care Excellence (NICE) recommended treatment options for the treatment of SeLECTS in children.

Clinical Trial Information

Trial	PMID: 11051123; Sulthiame as Monotherapy in Children with Benign Childhood Epilepsy with Centrotemporal Spikes: A 6-Month Randomized, Double-Blind, Placebo-Controlled Study. **Phase:** Not reported **Location (s):** Twenty-six European centres **Study completion date:** Not reported
Trial Design	Randomised, double-blinded and placebo-controlled
Population	N = 66 (actual); children aged 3 to 11 years with a diagnosis of BECTS, who have had two or more seizures in the last 6 months
Intervention(s)	STM, 5 mg/kg/day
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome measure: The rate of treatment failure events (TEFs) per group See trial record for a full list of other outcomes.
Results (efficacy)	Twenty-five of the 31 STM-treated patients (81%) and 10 of the 35 placebo-treated patients (29%) completed the trial without any TFEs (p = 0.00002).[2]
Results (safety)	STM was well tolerated. No patient was withdrawn for AEs.[2]

Trial	PMID: 23642492; Levetiracetam vs. sulthiame in benign epilepsy with centrotemporal spikes in childhood: A double-blinded, randomized, controlled trial (German HEAD Study). **Phase:** Not reported **Location (s):** Germany **Study completion date:** Not reported

Trial Design	Randomised, double-blinded and active comparator-controlled
Population	N = 44 (actual); children aged 6 to 12 years with a diagnosis of BECTS, who have had two or more seizures in the last 6 months
Intervention(s)	STM, 2 mg/kg body weight (initial dose). Further increased weekly by 2 mg/kg body weight
Comparator(s)	Levetiracetam (LEV), 10 mg/kg body weight (initial dose). Further increased weekly by 10 mg/kg body weight
Outcome(s)	Primary outcome measure: The rate of TEFs See trial record for a full list of other outcomes.
Results (efficacy)	TEFs occurred in four patients (19.0%) in the LEV treatment group and in two patients (9.1%) in the STM treatment group, respectively, (p = 0.412).[1]
Results (safety)	The total number of dropouts due to either seizure recurrence or adverse events was significantly higher in the LEV group (n = 9, 42.9%) compared to the STM group (n = 3, 13.6%, p = 0.03).[1]

Estimated Cost

The cost of sulthiame is not yet known.

Relevant Guidance

NICE Guidance

- NICE Guideline. Epilepsies in children, young people and adults (NG217). April 2022
- NICE Quality Standard. Epilepsies in children, young people and adults (QS211). December 2023
- NICE Interventional Procedure. Vagus nerve stimulation for refractory epilepsy in children. March 2004

NHS England (Policy/Commissioning) Guidance

- NHS England. National bundle of care for children and young people with epilepsy: annex 1 – Standards of care for children and young people with epilepsy. PRN00318_ii. March 2024

Other Guidance

No relevant guidance identified.

Additional Information

References

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