AWMSG Secretariat Assessment Report – Limited submission

Perampanel (Fycompa®) 2 mg, 4 mg, 6 mg, 8 mg, 10 mg and 12 mg film-coated tablets, and 0.5 mg/ml oral suspension

Company: Eisai Ltd

Licensed indication under consideration: Adjunctive treatment of partial-onset seizures (POS) with or without secondarily generalised seizures in patients from 4 to < 12 years of age.

In line with AWMSG's advice (2013) for use in patients aged 12 years and older, the company's submission focuses on a subpopulation of the licensed indication for the treatment of patients whose seizures are still uncontrolled with the first adjunctive therapy.

Date of licence extension: 10 November 2020

Comparator(s)

The comparators included in the company submission are:

- brivaracetam (Briviact®)
- eslicarbazepine acetate (Zebinix®)
- lacosamide (Vimpat®)
- zonisamide

Limited submission details

The limited submission criteria were met based on a minor licence extension

Clinical effectiveness

- In 2013, perampanel (Fycompa®) was recommended by the All Wales Medicines Strategy Group (AWMSG) as an option for restricted use within NHS Wales. Perampanel should be restricted to treatment of patients whose seizures are still uncontrolled with first adjunctive therapy, within its licensed indication as adjunctive treatment of partial-onset seizures with or without secondarily generalised seizures in patients with epilepsy aged 12 years and older.
- This submission covers the paediatric licence extension for children aged 4 to < 12 years and is restricted in line with AWMSG's advice for patients aged 12 years and older.
- The NICE pathway for epilepsy recommends seeking input from a tertiary epilepsy specialist when first adjunctive therapy for partial-onset seizures is ineffective or not tolerated. At this stage, treatment options for consideration include eslicarbazepine acetate, lacosamide, phenytoin, phenobarbital, vigabatrin and zonisamide. AWMSG has previously recommended eslicarbazepine acetate, brivaracetam and lacosamide for adjunctive treatment of partial-onset seizures with or without secondary generalisation in children. Based on clinical practice in

Wales and the available AWMSG advice the comparators for this submission seem appropriate.

- There is no direct head-to-head comparative evidence between perampanel and the comparators. The company submission includes results from one phase III open-label, uncontrolled study (study 311) using perampanel oral suspension as adjunctive therapy in children aged 4 to < 12 years (n = 180). The licence extension was also supported by a phase II open-label pilot study (Study 232) in children aged 2 to < 12 years with epilepsy (n = 50) which evaluated the pharmacokinetics of perampanel oral suspension and generated preliminary safety, tolerability and efficacy data.
- In study 311, children with partial-onset seizures with or without secondarily generalised seizures (n = 149) or primary generalised tonic-clonic seizures (n = 31) received perampanel oral suspension once daily in addition to their pre-study anti-epileptic medicines. The dose of perampanel was titrated over an 11-week period and then maintained over the following 12 weeks (core study). Patients who completed all scheduled visits during the core study were eligible to continue into an extension phase, which was a further 29 weeks (136 patients enrolled into the extension phase).
- The primary endpoint for study 311 was safety and tolerability. No new adverse events were reported. Forty percent of patients required a dose reduction, however, withdrawal due to treatment-emergent adverse events was < 10%. The overall safety profile is considered similar to that in adults and adolescents with the exception of somnolence, irritability, aggression and agitation, which were observed more frequently in study 311 compared to studies in adolescents and adults. The Committee for Medicinal Products for Human Use (CHMP) noted that this is consistent with the known safety profile of perampanel. This observation is highlighted in the Summary of Product Characteristics. Further studies are being undertaken to gather data on the longer term effects (> 12 months) on learning, intelligence, growth, endocrine function and puberty.
- Key secondary endpoints in study 311 included measures of efficacy. For the POS cohort at week 23 results were: a median change in seizure frequency per 28 days of −40.1%; a 50% or greater responder rate of 46.6%; a seizure free rate of 11.5%. The corresponding figures for the secondarily generalised seizures subgroup of the POS cohort were −58.7%, 64.8% and 18.5%, respectively. These figures are considered clinically meaningful and are comparable to results from studies in adults. CHMP noted that efficacy results observed in the extension phase of study 311 (and 232) were consistent with those observed in the core study.
- Evidence from studies 311 and 232 also support the licence extension to patients aged 4 to < 12 years for the tablet formulation. Data available indicate that the oral suspension and tablet formulations are bioequivalent at steady state. Dosing recommendations are the same for both formulations, though caution is advised if switching between the two.

Budget impact

- The company estimates that 273 children (aged 4 to < 12 years) are eligible for perampanel treatment in NHS Wales in the first year. This estimate is based on population data for Wales, prevalence and incidence data for the UK, and assumes that 55% of people with epilepsy have partial-onset seizures of which 30% need adjunctive therapy.
- The cost of treatment differs according to the patient's weight. The annual cost per patient for perampanel oral suspension and the comparators was calculated based on the average maintenance dose for each medicine.
- Based on the company's market share projections perampanel is assumed to partly displace all four comparators. The company estimates that [commercial in confidence figure removed] patients are likely to be prescribed perampanel oral suspension in Year 1 based on an anticipated uptake of [commercial in confidence figure removed], increasing to [commercial in confidence figure removed] patients in Year 5 based on an anticipated uptake of [commercial in confidence figure removed]. This leads to estimated net medicine acquisition costs of [commercial in confidence figure removed] in Year 1 and [commercial in confidence figure removed] in Year 5. The company's market share projections capture an estimate of the proportion of patients still uncontrolled despite first adjunctive therapy.
- The company has provided a sensitivity analysis varying the dose of perampanel oral suspension. Using the higher end of the maintenance dose range for patients aged < 12 years the net medicine acquisition costs for perampanel oral suspension are [commercial in confidence figure removed] in Year 1and [commercial in confidence figure removed] in Year 5.
- It is anticipated that the majority of patients aged < 12 years will receive treatment with the oral suspension formulation of perampanel. The submission also includes the tablet formulation. Perampanel tablets are associated with a Wales Patient Access Scheme and at the average maintenance dose the cost of the tablets is similar to the oral suspension.

Additional information

- AWTTC is of the opinion that, if recommended, perampanel (Fycompa®) for the indication under consideration may be appropriate for use within NHS Wales prescribed under specialist recommendation.

Evidence search

Date of evidence search: 11 February 2021
Date of range of evidence search: No date limits were applied to database searches.

Further information

This assessment report will be considered for review every three years.

References are available on request. Please email AWTTC at AWTTC@Wales.nhs.uk for further information.

This report should be cited as: All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report. Perampanel (Fycompa®) 2 mg, 4 mg, 6 mg, 8 mg, 10 mg and 12 mg film-coated tablets, and 0.5 mg/ml oral suspension. Reference number: 4770. April 2021.