AWMSG Secretariat Assessment Report – Limited submission

Lacosamide (Vimpat®) 50 mg, 100 mg, 150 mg, 200 mg film-coated tablets; 10 mg/ml syrup; 10 mg/ml solution for infusion

Company: UCB Pharma Ltd.

Licensed indication under consideration: Adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in children from ≥ 4 years of age to ≤ 15 years of age with epilepsy.

Date of licence extension: 14 September 2017

Comparator(s)

The comparators included in the company submission are:

- oxcarbazepine
- eslicarbazepine
- zonisamide.

Limited submission details

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

Clinical effectiveness

- This submission covers a licence extension for lacosamide to include its use as adjunctive therapy in the treatment of partial-onset seizures (POS) with or without secondary generalisation in children aged ≥ 4 to ≤ 15 years with epilepsy. The adjunctive use of lacosamide in patients aged 16 years and older has not been appraised by the All Wales Medicines Strategy Group (AWMSG) because it was licensed before 1 October 2010 and therefore was not on AWMSG's remit to appraise. Clinical expert opinion sought by the All Wales Therapeutics and Toxicology Centre (AWTTC) has confirmed that lacosamide is established in NHS Wales as adjunctive therapy in the treatment of partial-onset seizures in adults. Usage figures also obtained by AWTTC show that the medicine is in use in NHS Wales.
- Treatment choice in epilepsy is guided by a number of factors including patient co-morbidities, concurrent medications, medicine tolerability and formulation(s) available. Clinical experts in Wales have confirmed that in general they would expect to use lacosamide as third-line treatment, that is, after failure of monotherapy and first-line adjunctive therapy. Clinical experts also indicated that lacosamide may be used second-line where first-line adjunctive agents cannot be used. It is therefore expected that lacosamide would potentially displace eslicarbazepine or zonisamide, although clinical expert opinion suggests that eslicarbazepine is not commonly used in paediatrics.
- In line with National Institute for Health and Clinical Excellence Clinical Guideline 137, oxcarbazepine is generally used before lacosamide, eslicarbazepine and zonisamide. The applicant company has acknowledged that oxcarbazepine is not

a major comparator and this is reflected by their low market share projections for oxcarbazepine.

- The paediatric licence extension was based on the extrapolation of efficacy data from clinical studies in patients aged 16 years and above, with additional supportive data regarding the dosage and safety of lacosamide in children aged 4 years and above. The European Medicines Agency has endorsed the extrapolation of efficacy results of anti-epileptic medicines in adults to children via a reflection paper on extrapolation in paediatric medicine development and a guideline on the clinical investigation of epilepsy-specific medicinal products.
- Three multicentre, double-blind, randomised, placebo-controlled studies (SP667, SP754, SP755) in patients 16–70 years of age as well as interim data from a double-blind, randomised, placebo-controlled phase III study (SP0969) to assess safety, tolerability and efficacy of adjunctive lacosamide treatment in 340 children aged 4–16 years with uncontrolled POS have been assessed. Pooled results from the three studies in patients aged 16–70 years of age showed that adjunctive treatment with lacosamide significantly increased the percentages of patients who experienced a 50% greater reduction in seizure frequency: 34% of those receiving 200 mg/day lacosamide and 40% of those receiving 400 mg/day lacosamide compared with 23% of those receiving placebo. In addition, statistically significant reductions in seizure frequency from baseline to the end of the maintenance period (12 weeks) that were 14–28% greater than those seen with placebo. Interim data (at 96 weeks) from the study in children showed that those treated with adjunctive lacosamide had 32% greater reduction in seizure frequency per 28 days from baseline relative to placebo; and 53% of those in the lacosamide group had at least a 50% reduction in seizure frequency per 28 days from baseline to the end of the maintenance period (10 weeks) compared with 33% of the placebo group.
- A Bayesian network meta-analysis (NMA) of relevant randomized controlled trials of adjunctive therapy of POS in adults showed that lacosamide had comparable efficacy to all three comparators (oxcarbazepine, eslicarbazepine and zonisamide) in achieving at least a 50% reduction in seizure frequency from baseline to treatment period. The systematic review used to inform the NMA only included publications up to November 2014 and a small number of trials (n=3) for lacosamide.
- Interim safety and tolerability data from two ongoing studies (EP0034 and SP848) in children aged from 1 month to ≤ 17 years showed that observations were as expected for the paediatric population; most adverse events were either mild or moderate and no new safety concerns were identified. The CHMP concluded that the safety profile observed in patients aged 4 years and over was generally consistent with that seen in adults. As part of the risk management plan for lacosamide, studies are ongoing investigating its impact on long-term growth, neurodevelopment, and on puberty.
- Lacosamide is available in a number of different formulations, film-coated tablets, an oral syrup, and an intravenous formulation. This provides an option for children who find it difficult to swallow and if children are unable to take oral medicines without the need to change medication when changing formulations.

Budget impact

- The company estimates that 182 children (aged ≥ 4 to ≤ 15 years) are eligible for lacosamide treatment in NHS Wales in the first year, based on population data for Wales, prevalence data for the UK and incidence data from the epidemiology of epilepsy in Europe and assumes that 35% of people with epilepsy have partial-onset seizures and 30% of these would need adjunctive therapy.
- The cost of treatment differs according to the weight of the patient. To account for this the annual cost per patient for lacosamide and each of the comparators was

calculated using median weight data for each age within the range ≥ 4 to ≤15 years and Welsh population size data for the relevant age range.

- Based on the company's market share projections lacosamide is assumed to partly displace all three comparators (zonisamide 39.1%; oxcarbazepine 5.3%; eslicarbazepine 55.6%), with an estimated four patients being eligible for treatment with lacosamide in Year 1 based on an anticipated uptake of 2% increasing to 24 patients in Year 5 based on an anticipated uptake of 8%. The company estimates that this will result in net medicine acquisition cost savings of £4 in Year 1 to £1,546 in Year 5.
- The company also provided an additional scenario analysis to account for low market share projections for eslicarbazepine, as requested by AWTTC in light of feedback from clinical experts (zonisamide 89.4%; oxcarbazepine 5.3% and eslicarbazepine 5.3%). In this scenario using the same number of eligible patients and anticipated percentage uptake of lacosamide as above, resulted in net medicine acquisition cost savings of £536 in Year 1 and a net medicine acquisition cost of £2,463 in Year 5.

Additional information

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

- The company does not anticipate that lacosamide (Vimpat®) will be supplied by a home healthcare provider.

Evidence search

Date of evidence search: 23-24 October 2017
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. Lacosamide (Vimpat®) 50 mg, 100 mg, 150 mg, 200 mg film-coated tablets; 10 mg/ml syrup; 10 mg/ml solution for infusion. Reference number: 3343. February 2017.