EMA/612892/2018
Human Medicines Evaluation Division

Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

Vimpat

lacosamide

Procedure no: EMEA/H/C/000863/P46/029

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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1. Introduction

On 11 of June, 2018, the MAH submitted the results of EP0045 study in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

Based on the new data presented in this Clinical Overview and the corresponding EP0045 clinical study report (CSR), the MAH is not seeking to expand the current label in paediatrics with this submission. Furthermore, the data do not influence the benefit risk balance of lacosamide (LCM) to require any regulatory action on the marketing authorization of Vimpat. The benefit-risk of LCM remains positive.

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

The MAH stated that EP0045 a multicentre, prospective, single-arm non-interventional study (NIS) conducted at specialized sites utilizing LCM added to existing treatment with 1 or 2 Baseline antiepileptic drugs (AEDs) in patients ≥16 years of age with brain tumor related epilepsy (BTRE) secondary to low-grade glioma is a stand-alone study (NCT02276053).

2.2. Information on the pharmaceutical formulation used in the study

Patients were treated with commercially available LCM.

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for:

- EP0045: a non-interventional study of Vimpat (Lacosamide) as adjunctive antiepileptic drug therapy in patients with brain tumor-related epilepsy (BTRE) (VIBES) (NCT02276053);

Lacosamide belongs to a novel class of functionalized amino acids. It was first approved by the European Medicines Agency in 2008 and is indicated as monotherapy and adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalization in adults, adolescents, and children from 4 years of age with epilepsy (tablets, syrup, and solution for intravenous infusion). In the United States, LCM has been approved as monotherapy and adjunctive therapy in the treatment of partial-onset seizures in patients 4 years of age and older for tablets and oral solution, and 17 years of age and older for intravenous infusion.

2.3.2. Clinical study

EP0045; a non-interventional study of Vimpat (lacosamide) as adjunctive antiepileptic drug therapy in patients with brain tumor-related epilepsy (BTRE) (VIBES) (NCT02276053).

Description

Methods

Objective(s)

Primary objective

The primary objective of this NIS was to evaluate the effectiveness and patient global impression of change (PGIC) of LCM added to 1 or 2 AEDs in the treatment of patients with BTRE due to low-grade primary brain tumor.

Secondary objective

The secondary objective of this NIS was to evaluate the tolerability and quality of life (QoL) of patients with BTRE due to low-grade primary brain tumor who were treated with LCM added to 1 or 2 AEDs.

Study design

EP0045 was a multicenter, prospective, single-arm NIS conducted at specialized sites utilizing LCM added to existing treatment with 1 or 2 Baseline AEDs in patients ≥16 years of age with BTRE secondary to low-grade tumor.

The patients were to be followed as per current clinical practice for their condition. No additional diagnostic or monitoring procedures were to be applied. The choices of AED treatment were to be made independently by the treating physician in the regular course of practice and were, therefore, independent of participation in this NIS.

Eligible patients were enrolled consecutively and all patients (and/or their parents or legal representatives) had to accept in writing that his/her medical data would be used for the evaluation of the study results by signing a study-specific Patient Data Consent form according to local requirements.

The clinical evaluation of patients with BTRE secondary to low-grade glioma was performed by the treating physician following routine clinical practice. All visits and assessments were scheduled and conducted per routine clinical practice. It was anticipated that visits would occur every 3 months based on standard of care; therefore, each patient would have approximately 3 visits during their participation in this study. These visits consisted of:

- Visit 1, Baseline
- Visit 2, approximately 3 months after Baseline according to routine practice
- Visit 3, approximately 6 months after Baseline according to routine practice or end of Observation Period

The Observation Period per patient was planned to be up to 6 months after initiation of LCM treatment. Patients who discontinued early had to perform Visit 3 assessments as a Withdrawal Visit.

Treatments

Patients were treated with commercially available LCM and with commercially available AEDs, as prescribed by treating physicians, in accordance with current clinical practice. LCM was added to any existing AED therapies that the patient was taking.

Outcomes/endpoints

Primary efficacy variable

The following primary variables were measured:

- Response at the end of the 6-month Observation Period, where a responder was a patient experiencing a 50% or greater reduction in partial-onset seizure frequency from Visit 1 (Baseline) to Visit 3 (Month 6 or end of Observation Period)
- Patient Global Impression of Change rating at Visit 3 (Month 6 or end of Observation Period)

The following safety variables were collected:

- Occurrence of ADRs or AESIs spontaneously reported by the patient or observed by the treating physician
- Patient withdrawal due to ADRs

For the assessment of safety of LCM, the causal relationship, seriousness, and outcome of ADRs and AESIs were collected during the Observation Period. It was the task of the treating physician to make a judgment about a causal relationship with the LCM intake.

Statistical Methods

All statistical analyses were performed in an exploratory manner.

Results

Recruitment/ Number analysed

A total of 93 patients were enrolled into the EP0045 study. This document summarizes disposition and treatment emergent adverse events (TEAEs) for the 1 subject from EP0045 study who was <18 years old at the time of study entry in order to fulfil the requirement of reporting paediatric data as outlined in Article 46.

Baseline data

Subject [Protected Personal Data removed] was a 16 year-old male who had a Grade 1 craniopharyngiome with partial onset seizures with secondary generalization. Seizure frequency per 28 days at Baseline was 1.50. The subject used the concomitant AEDs clobazam and levetiracetam during the study.

Efficacy results

The subject completed the study after 175 days of treatment with LCM in EP0045. Subject [Protected Personal Data removed] was seizure free at Visit 3.

Safety results

No TEAEs were reported for Subject [Protected Personal Data removed] during the study.

2.3.3. Discussion on clinical aspects

There was only one patient <18 years old included into the EP0045 study. The patient was seizure free at the end of the study period when he was treated with adjunctive treatment with LCM (in addition to clobazam and levetiracetam). The safety profile of this one subject <18 years old in EP0045 was consistent with the established profile of LCM in subjects with partial-onset seizures with and without secondary generalization. No new safety concerns were identified in this subject.

3. Rapporteur's overall conclusion and recommendation

The results of EP0045 study are being submitted in accordance with Article 46 of Regulation (EC) No 1901/2006 (The Paediatric Regulation). The MAH proposed no changes to the approved EU Summary of Product Information for Vimpat with this submission based on EP0045 study results. The MAH proposal is supported by the Rapporteur.

☒ **Fulfilled:**

No regulatory action required.

4. Additional clarification requested

Not applicable.