



UCB
News

UCB's anti-epileptic drug VIMPAT® (lacosamide) receives positive opinion by EU CHMP as monotherapy for patients with partial-onset seizures

- CHMP positive opinion, pending EU Commission approval, takes us one step closer to VIMPAT® being approved as monotherapy for patients with partial-onset seizures
- EU Commission approval would broaden VIMPAT® clinical application in Europe, strengthening UCB's leadership in epilepsy and commitment to improving the lives of people with epilepsy

Brussels (Belgium), 11th November 2016 1800 (CET): The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has today adopted a positive opinion on a license extension for UCB's epilepsy medicine VIMPAT® (lacosamide) for use as monotherapy in the treatment of partial-onset seizures in patients with epilepsy aged 16 years and older.¹ The European Commission's approval decision is expected in the first quarter of 2017.

The CHMP positive opinion was supported by a Phase III international, double-blind, randomized, active-controlled, non-inferiority trial, conducted according to guidance issued by the EMA and the International League Against Epilepsy, results of which were previously presented at the European Academy of Neurology and European Congress on Epileptology meetings earlier this year.^{2,3,4,5} Results from the study are expected to be published during November 2016 within *The Lancet Neurology*.

"Choosing the first antiepileptic drug (AED) is of utmost importance for patients with newly diagnosed disease – since they will most likely need long-term therapy, the AED must be effective, well-tolerated, have low potential for drug–drug interactions, and suit their disease and lifestyle profiles", explained Professor Michel Baulac, Hôpital de la Pitié-Salpêtrière, Paris, France. *"When we try to select an existing monotherapy option for patients based on their profile and the attributes of the AED, we are left with few choices. Consequently, adoption of a positive opinion by CHMP, recommending approval of lacosamide as monotherapy, represents a major advance in terms of new options for people with epilepsy and of possibilities to tailor treatment to the individual patient."*

The lifetime prevalence of epilepsy is 2-5% and seizure incidence rates tend to be higher in people over the age of 65.⁶ An estimated seven million people in Europe will have an epileptic seizure at some time during their lives, and as many as 30% may have a treatment-refractory form of the condition.⁶ This CHMP positive opinion takes us one step closer to VIMPAT® being approved as

monotherapy for patients with partial-onset seizures and, pending approval, could provide an additional treatment option for this patient population, representing a significant unmet need.⁷

“Epilepsy can affect people in many different ways, and a range of treatment options are required to ensure that therapy is tailored to a person’s individual needs. UCB is committed to making VIMPAT[®] available to help more people living with epilepsy worldwide,” explained Jeff Wren, Head of UCB’s Neurology Patient Value Unit. *“The CHMP’s positive opinion builds on our longstanding commitment to help people with seizure disorders at every point of their journey.”*

Currently VIMPAT[®] is approved in 44 countries as adjunctive therapy for the treatment of partial-onset seizures in adults with epilepsy (ages ≥ 17 years in the U.S.,⁸ ages ≥ 16 years in the EU⁹), and is already licenced as monotherapy in the US (ages ≥ 17 years⁸). VIMPAT[®] peak sale expectations are confirmed to reach at least €1.2 billion by 2020.

About VIMPAT[®]

VIMPAT[®] (lacosamide) was first launched in the European Union in September 2008, as adjunctive therapy for the treatment of partial-onset seizures with or without secondary generalization in adult and adolescent (16-18 years) patients with epilepsy. In countries of the EU, VIMPAT[®] is available as film-coated tablets, syrup and solution for infusion. VIMPAT[®] solution for infusion is an alternative for patients when oral administration is temporarily not feasible. VIMPAT[®] tablets and injection were launched in the U.S. in May 2009 as an add-on therapy for the treatment of partial-onset seizures in people with epilepsy who are aged 17 years and older. VIMPAT[®] injection is a short-term replacement when oral administration is not feasible in these patients. VIMPAT[®] oral solution was launched in the U.S. in June 2010. The availability of the oral tablets, oral solution, and intravenous (IV) injection allows for consistent patient treatment. In Asia, VIMPAT[®] is available in Korea, Hong Kong, Malaysia, Philippines and Thailand, and was recently approved for use in Japan, where the product will be jointly commercialized by Daiichi Sankyo. VIMPAT[®] is not approved in China. Important safety information about VIMPAT[®] is available below.

About Epilepsy^{10,11}

Epilepsy is a disease of the brain affecting approximately 65 million people worldwide. It is defined as either the occurrence of two or more unprovoked seizures >24 hours apart or one unprovoked (or reflex) seizure and a probability of further seizures occurring over the next 10 years that is similar to the general recurrence risk (at least 60%) after two unprovoked seizures or diagnosis of an epilepsy syndrome. Although epilepsy may be linked to factors such as health conditions, race and age, it can develop in anyone at any age, and approximately 1 in 26 people will develop epilepsy in their lifetime.

About UCB in Epilepsy

UCB has a rich heritage in epilepsy with over 20 years of experience in the research and development of novel antiepileptic drugs. Every day, thousands of people use AEDs from our portfolio to help control their seizures. As a company with a long-term commitment to epilepsy research our goal is to address unmet medical needs and to deliver solutions that improve patients’ lives. Our scientists are proud to contribute to advances in the understanding of epilepsy and its treatment. We partner and create super-networks with world-leading scientists and clinicians in academic institutions, pharmaceutical companies and other organizations who share our goals. At

UCB, we are inspired by patients and driven by science in our commitment to support patients with epilepsy.

About UCB

UCB, Brussels, Belgium (www.ucb.com) is a global biopharmaceutical company focused on the discovery and development of innovative medicines and solutions to transform the lives of people living with severe diseases in immunology and neurology. With more than 7,500 people in approximately 40 countries, the company generated revenue of €3.9 billion in 2015. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news

Important safety information about VIMPAT[®] in the EU and EEA

VIMPAT[®] is indicated as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalization in adult and adolescent (16-18 years) patients with epilepsy. VIMPAT[®] therapy can be initiated with either oral or IV administration. A single loading dose may be initiated in patients in situations when the physician determines that rapid attainment of VIMPAT[®] steady state plasma concentration and therapeutic effect is warranted. It should be administered under medical supervision with consideration of the potential for increased incidence of CNS adverse reactions. Administration of a loading dose has not been studied in acute conditions such as status epilepticus. Contraindications: Hypersensitivity to the active substance or any of the excipients; known second- or third-degree atrioventricular (AV) block. Special warnings and precautions for use: Treatment with VIMPAT[®] has been associated with dizziness which could increase the occurrence of accidental injury or falls. Therefore, patients should be advised to exercise caution until they are familiar with the potential effects of the medicine. Prolongations in PR interval with VIMPAT[®] have been observed in clinical studies. Cases with second- and third-degree AV block associated with VIMPAT[®] treatment have been reported in post-marketing experience. VIMPAT[®] should be used with caution in patients with known conduction problems or severe cardiac disease such as a history of myocardial infarction or heart failure. Caution should especially be exerted when treating elderly patients as they may be at an increased risk of cardiac disorders or when VIMPAT[®] is used in combination with products known to be associated with PR prolongation. In the placebo-controlled trials of VIMPAT[®] in epilepsy patients, atrial fibrillation or flutter were not reported; however both have been reported in open-label epilepsy trials and in post-marketing experience. Patients should be made aware of the symptoms of second-degree or higher AV block (e.g. slow or irregular pulse, feeling lightheaded and fainting) and of the symptoms of atrial fibrillation and flutter (e.g. palpitations, rapid or irregular pulse, shortness of breath). Patients should be counselled to seek medical advice should any of these symptoms occur. Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic agents in several indications. Therefore patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behaviour emerge. VIMPAT[®] syrup contains sodium methyl parahydroxybenzoate (E219) which may cause allergic reactions (possibly delayed). It contains 3.7 g sorbitol (E420) per dose (200 mg VIMPAT[®]), corresponding to a calorific value of 9.7 kcal. Patients with rare hereditary problems of fructose intolerance should not take this medicine. The syrup contains aspartame (E951), a source of phenylalanine, which may be harmful for people with phenylketonuria. VIMPAT[®] syrup and the solution for infusion contain sodium, which should be taken into consideration for patients on a

controlled sodium diet. Effects on ability to drive and use machines: VIMPAT[®] may have minor to moderate influence on the ability to drive and use machines. VIMPAT[®] treatment has been associated with dizziness or blurred vision. Accordingly patients should be advised not to drive a car or to operate other potentially hazardous machinery until they are familiar with the effects of VIMPAT[®] on their ability to perform such activities. Undesirable effects: The most common adverse reactions ($\geq 10\%$) are dizziness, headache, diplopia, and nausea. They were usually mild to moderate in intensity. Some were dose-related and could be alleviated by reducing the dose. Incidence and severity of CNS and gastrointestinal (GI) adverse reactions usually decreased over time. Incidence of CNS adverse reactions such as dizziness may be higher after a loading dose. Other common adverse reactions ($\geq 1\%$ - $< 10\%$) are depression, confusional state, insomnia, balance disorder, coordination abnormal, memory impairment, cognitive disorder, somnolence, tremor, nystagmus, hypoesthesia, dysarthria, disturbance in attention, paraesthesia, vision blurred, vertigo, tinnitus, vomiting, constipation, flatulence, dyspepsia, dry mouth, diarrhoea, pruritus, rash, muscle spasms, gait disturbance, asthenia, fatigue, irritability, feeling drunk, injection site pain or discomfort (local adverse events associated with intravenous administration), irritation (local adverse events associated with intravenous administration), fall, and skin laceration, contusion. The use of VIMPAT[®] is associated with dose-related increase in the PR interval. Adverse reactions associated with PR interval prolongation (e.g. atrioventricular block, syncope, bradycardia) may occur. Laboratory abnormalities: Abnormalities in liver function tests have been observed in controlled trials with VIMPAT[®] in adult patients with partial-onset seizures who were taking 1-3 concomitant antiepileptic drugs. Elevations of ALT to ≥ 3 XULN occurred in 0.7% (7/935) of VIMPAT[®] patients and 0% (0/356) of placebo patients. Multiorgan Hypersensitivity Reactions: Multiorgan hypersensitivity reactions (also known as Drug Reaction with Eosinophilia and Systemic Symptoms, DRESS) have been reported in patients treated with some antiepileptic agents. These reactions are variable in expression but typically present with fever and rash and can be associated with involvement of different organ systems. If multiorgan hypersensitivity reaction is suspected, VIMPAT[®] should be discontinued.

Refer to the European Summary of Product Characteristics for other adverse reactions and full prescribing information. Date of revision: 30 July 2015 <http://www.ema.europa.eu/>.

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References

¹ European Medicines Agency. Accessed 11th November from http://www.ema.europa.eu/docs/en_GB/document_library/Summary_of_opinion/human/000863/WC500216004.pdf

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- ² Baulac, M. et al., Efficacy and tolerability of lacosamide monotherapy in patients with newly diagnosed epilepsy: A randomized double-blind trial versus controlled-release carbamazepine. Eur J Neurol;6-23-2016;23;Suppl 2;52, abs 0122. 22nd Congress of the European Academy of Neurology (EAN), May 28-31, 2016;Copenhagen, Denmark
- ³ Toledo M. et al. Efficacy of lacosamide monotherapy in patients with newly diagnosed epilepsy stratified by baseline disease severity: subanalysis of data from a prospective noninferiority trial versus controlled-release carbamazepine. Poster presented at 12th European Congress on Epileptology (ECE), September 11 to 15, 2016; Prague, Czech Republic
- ⁴ Baulac M. et al. Efficacy and tolerability of lacosamide monotherapy in patients with newly diagnosed epilepsy: A prospective randomized double-blind non-inferiority trial versus controlled-release carbamazepine. Presented at 12th European Congress on Epileptology (ECE), September 11 to 15, 2016; Prague, Czech Republic
- ⁵ Rosenow F. et al. Efficacy and tolerability of monotherapy with lacosamide versus controlled-release carbamazepine in elderly patients with newly diagnosed epilepsy: a subgroup analysis of a prospective randomized double-blind trial. Poster presented at 12th European Congress on Epileptology (ECE), September 11 to 15, 2016; Prague, Czech Republic
- ⁶ European Federation of Pharmaceutical Industries and Associations. Epilepsy. Accessed 10th November 2016 from <http://www.efpia.eu/diseases/89/59/Epilepsy>
- ⁷ Schmidt D, Schachter SC. Drug treatment of epilepsy in adults. BMJ. 2014;348:g2546 (<https://www.ncbi.nlm.nih.gov/pubmed/24583319>)
- ⁸ U.S. Food and Drug Administration. VIMPAT[®] (lacosamide) Prescribing Information. Accessed 11th November 2016 from http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/022255s026s027,022254s019s020,022255s012s013lbl.pdf
- ⁹ European Medicines Agency, Summary of Product Characteristics. Accessed 11th November 2016 from http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000863/WC500050338.pdf
- ¹⁰ The Epilepsy Foundation of America. Who gets epilepsy? Accessed 11th November 2016 from <http://www.epilepsy.com/learn/epilepsy-101/who-gets-epilepsy>
- ¹¹ Fisher, R.S., et al., ILAE Official Report: A practical clinical definition of epilepsy. Epilepsia, 2014. 55(4):475-482.

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