UCB News

UCB's anti-epileptic drug VIMPAT® (lacosamide) approved as monotherapy by European Commission

- **European monotherapy indication broadens clinical application of VIMPAT® for people with epilepsy living with partial-onset seizures**

Brussels (Belgium), 20th December 2016 – 0700 (CET): The European Commission (EC) has approved a license extension for UCB's anti-epilepsy drug (AED) VIMPAT® (lacosamide) for use as monotherapy in the treatment of partial-onset seizures (POS) in adult and adolescent (16-18 years) patients with epilepsy.[1] The approval comes into immediate effect, following a positive opinion recommendation from the Committee for Medicinal Products for Human Use (CHMP) in November 2016[2].

The Commission's decision approval was supported by a Phase III international, double-blind, randomized, active-controlled, non-inferiority trial, which showed non-inferiority of lacosamide (VIMPAT®) monotherapy compared with controlled-release carbamazepine among patients with newly or recently diagnosed POS. The trial, published in the November edition of the *Lancet Neurology*[3], was conducted according to guidance issued by the EMA and the International League Against Epilepsy and involved 888 patients aged 16 years or older making it the largest trial of its kind so far. Lacosamide was generally well tolerated by patients, with an adverse event (AE) profile comparable to that observed in previous trials, including dizziness, headache and nausea.

"*We are delighted that, with this new monotherapy indication for VIMPAT®, it will now be available to help even more patients living with partial onset epilepsy,*" explained Jeff Wren, Head of UCB's Neurology Patient Value Unit. "*Bringing new epilepsy solutions to support people living with epilepsy has been a core UCB mission over the last decade. This monotherapy indication builds on our longstanding commitment to help people with seizure disorders at every point of their journey*."

The lifetime prevalence of epilepsy is 2-5%, and seizure incidence rates tend to be higher in people over the age of 65. 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.[4] This Commission decision provides an additional treatment option for people with epilepsy, representing a significant unmet need.[5]

"Selection of the first antiepileptic drug is one of the most important decisions for patients – together, we need to choose one that is effective, is generally well tolerated, and suits their individual profile" explained Professor Michel Baulac, Hôpital de la Pitié-Salpêtrière, Paris, France and lead author of the recent *Lancet Neurology* paper. *"Epilepsy is a complex multifactorial disease and not all patients will respond to currently available options; consequently, addition of another antiepileptic drug to the selection we can choose is very important."*

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.,[6] ages ≥ 16 years in the EU[1]), and has been approved as monotherapy in the US (ages ≥ 17 years[6]) since 2014. 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[7,8]

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 the Phase III international, double-blind, randomized, active-controlled trial [3]

Results are from a Phase III international, double-blind, randomized, active-controlled trial, the fourth in a series of non-inferiority trials conducted according to guidance issued by the European Medicines Agency and the International League Against Epilepsy, were recently published in the prestigious *Lancet Neurology* journal.[3]

Overall, 888 patients aged 16 years or older took part in the study, making it the largest trial of its kind so far. Six-month seizure-freedom, the primary endpoint of the trial, was 91.5% among patients treated with lacosamide (200–600mg/day) and 92.8% with carbamazepine-CR (400–1200mg/day). Kaplan-Meier estimates for these rates, based on the proportion of patients completing six months of treatment at the last evaluated dose without experiencing a seizure, were 73.6% and 69.7%, respectively. The adverse event (AE) profile was comparable to that observed in previous lacosamide trials, including dizziness, headaches and nausea.

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

About VIMPAT® (lacosamide)

Important Safety Information about VIMPAT® in the EU and EEA

VIMPAT® (lacosamide) is indicated as monotherapy and 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 lacosamide 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. Dose-related 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, severe cardiac disease (e.g. history of myocardial infarction or heart failure), in elderly patients, or when VIMPAT® is used in combination with products known to be associated with PR prolongation. In these patients it should be considered to perform an ECG before a Vimpat dose increase above 400mg/day and after Vimpat is titrated to steady-state. 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 of 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 counseled 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 lacosamide), 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 (≥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 (≥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 ≥3XULN 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: 12 December 2016

http://www.ema.europa.eu/

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