UCB News

UCB's anti-epileptic drug VIMPAT® (lacosamide) receives EU approval for paediatric use

- VIMPAT® is approved for monotherapy and adjunctive therapy of partial-onset (focal) seizures in children aged 4 years and older and now provides a new treatment choice for physicians and their paediatric patients with epilepsy.[1]
- Epilepsy is the most common serious neurological disorder among children and young adults with the prevalence of paediatric epilepsy in Europe ranging from 3.2 – 5.1 per 1,000.[2]
- Despite its high prevalence, approximately 10 – 29% of paediatric epilepsy patients experience inadequate seizure control with currently available anti-epileptic drugs.[3,4]

Brussels (Belgium), 21 September 2017 – 18:00 (CEST): UCB today announced that the European Commission (EC) approved expanding the use of its anti-epileptic drug (AED) VIMPAT® (lacosamide) as monotherapy and adjunctive therapy in the treatment of partial-onset seizures (also known as focal-onset seizures (FOS) according to ILAE terminology [5,6]) with or without secondary generalisation in adults, adolescents and children from 4 years of age.[1]

The approval follows a positive opinion adopted in July by the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA), and provides a new treatment option to aid the management of childhood epilepsy.[7]

"Today's approval of VIMPAT® for children aged 4 to 16 is an important step forward for the management of paediatric epilepsy, a condition which can present significant challenges to children and their families," said Jeff Wren, Executive Vice-President, Head of UCB's Neurology Patient Value Unit. *"One of our key commitments at UCB is to improve the lives of people with epilepsy, and we are proud to be providing a proven treatment option for this highly impacted patient population."*

Epilepsy is a common, chronic neurological disorder, affecting approximately 65 million people worldwide,[8] with almost half of incident cases diagnosed during childhood.[9] There are a number of comorbidities in childhood that may be associated with epilepsy, including cognitive impairment and neuropsychiatric conditions, mood disorders, and physical comorbidities.[10] The stigma

associated with epilepsy, especially during adolescence, has been related to low self-esteem, worry, and negative feelings about life,[11] with 12 – 26% of children with epilepsy reporting depression and anxiety.[12] Paediatric patients may suffer from adverse events with currently available AEDs.[13] As such, there is a need for additional treatment options that may provide seizure control with a low side effect profile.

"*Paediatric patients with focal seizures can still experience poor seizure control with currently available treatment options, along with a reduced quality of life*," said Professor Alexis Arzimanoglou, Coordinator of the Epilepsy Program of the Epilepsy Unit at San Juan de Deu Barcelona Children's University Hospital and Director of the Paediatric Clinical Epileptology, Sleep disorders and Functional Neurology Department at the University Hospitals of Lyon, France. "*With the approval of lacosamide, healthcare professionals and paediatric patients in the EU now have an additional treatment option for focal onset seizures, either as monotherapy or adjunctive therapy, representing a great advance to further help children aged 4 years and older suffering from epilepsy*."

The approval of VIMPAT® is based on the principle of extrapolation of its efficacy data from adults to children, and is supported by safety and pharmacokinetics data collected in children. The EMA has established that focal epilepsies in children older than 4 years old have a similar clinical expression to that in adolescents and adults.[14] The Food and Drug Administration (FDA) and EMA allow extension of indication to paediatric populations using extrapolated data provided the dose is established and the safety is demonstrated. The EMA states that, from the safety viewpoint, a minimum of 100 children treated by the study drug should be followed for at least one year.[14]

VIMPAT® has over 1,056,500 patient-years of exposure.[15] Its established efficacy, safety and tolerability of adjunctive therapy in adults with focal seizures has been demonstrated by three double-blind and three open-label extension studies.[16,17,18,19,20,21] The efficacy, safety and tolerability profile of first-line VIMPAT® monotherapy has been demonstrated in a phase 3, double-blind study and a related open-label extension study.[22]

VIMPAT® is approved in 72 countries worldwide. In the EU, it is also approved as monotherapy and adjunctive therapy for the treatment of partial-onset seizures (POS) with or without secondary generalisation in adults and adolescents (16 – 18 years) with epilepsy.[23] In the US, VIMPAT® is approved as monotherapy or adjunctive therapy for the treatment of POS in adults with epilepsy (ages ≥ 17 years).[24]

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 generalisation 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 US 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 approved for use in Japan in 2016, where the product will be jointly commercialised by Daiichi Sankyo. VIMPAT® is not approved in China. Important safety information about VIMPAT® is available below.

About Epilepsy[8,25]
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 longstanding commitment to improving the lives of people with epilepsy around the world. With over 20 years of experience in the research and development of antiepileptic drugs, our goal is to become a preferred partner for the global epilepsy community, improving knowledge about and access to effective solutions to help patients better manage their individual epilepsy journeys. We strive to 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 people 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 of the immune system or of the central nervous system. With more than 7500 people in approximately 40 countries, the company generated revenue of €4.2 billion in 2016. 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 monotherapy and adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 4 years of age with epilepsy. VIMPAT® therapy can be initiated with either oral or IV administration. For the paediatric population, the physician should prescribe the most appropriate formulation and strength according to weight and dose. 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. Use of a loading dose is not recommended in adolescents and children weighing less than 50 kg. A maximum dose of 300 mg/day is recommended for paediatric patients weighing 50 kg or more and for adult patients with mild to moderate hepatic impairment. Based on data in adults, in paediatric patients weighing less than 50 kg with mild to moderate hepatic impairment, a reduction of 25 % of the maximum dose should be applied. Lacosamide should be administered to adult and paediatric patients with severe hepatic impairment only when the expected therapeutic benefits are anticipated to outweigh the possible risks. The dose may need to be adjusted while carefully observing disease activity and potential side effects in the patient. In adolescents and adults weighing 50 kg or more with mild to moderate hepatic impairment a loading dose of 200mg may be considered, but further dose titration (>200 mg daily) should be performed with caution. In paediatric patients weighing 50 kg or more and in adult patients with mild or moderate renal impairment a loading dose of 200 mg may be considered, but further dose titration (> 200 mg daily) should be performed with caution. In paediatric patients weighing 50 kg or more and in adult patients with severe renal impairment (CLCR ≤ 30 ml/min) or with end-stage renal disease, a maximum dose of 250 mg/day is recommended and the dose titration should be performed with caution. In paediatric patients weighing less than 50 kg with severe renal impairment (CLCR ≤ 30 ml/min) and in those with end-stage renal disease, a reduction of 25 % of the maximum dose is recommended. 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 antiepileptic medicinal products 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. The safety and efficacy of lacosamide in paediatric patients with epilepsy syndromes in which focal and generalised seizures may coexist have not been determined. 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. The safety profile of lacosamide in open-label studies in adjunctive therapy in children from 4 years to less than 16 years was consistent with the safety profile observed in adults. In the paediatric population the most frequently reported adverse

reactions were vomiting (17.1 %), dizziness (16.7 %), somnolence (12.1 %), headache (11.7 %) and convulsion (10.1 %). Additional adverse reactions reported in children were decreased appetite (6.6 %), lethargy (4.3 %) and abnormal behaviour (1.9 %). 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 medicinal products. 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 medicinal products. 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: 14th September 2017 http://www.ema.europa.eu/.

Forward looking statements
This press release contains forward-looking statements based on current plans, estimates and beliefs of management. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial information, expected legal, political, regulatory or clinical results and other such estimates and results. By their nature, such forward-looking statements are not guarantees of future performance and are subject to risks, uncertainties and assumptions which could cause actual results to differ materially from those that may be implied by such forward-looking statements contained in this press release. Important factors that could result in such differences include: changes in general economic, business and competitive conditions, the inability to obtain necessary regulatory approvals or to obtain them on acceptable terms, costs associated with research and development, changes in the prospects for products in the pipeline or under development by UCB, effects of future judicial decisions or governmental investigations, product liability claims, challenges to patent protection for products or product candidates, changes in laws or regulations, exchange rate fluctuations, changes or uncertainties in tax laws or the administration of such laws and hiring and retention of its employees. UCB is providing this information as of the date of this press release and expressly disclaims any duty to update any information contained in this press release, either to confirm the actual results or to report a change in its expectations.
There is no guarantee that new product candidates in the pipeline will progress to product approval or that new indications for existing products will be developed and approved. Products or potential products which are the subject of partnerships, joint ventures or licensing collaborations may be subject to differences between the partners. Also, UCB or others could discover safety, side effects or manufacturing problems with its products after they are marketed.
Moreover, sales may be impacted by international and domestic trends toward managed care and health care cost containment and the reimbursement policies imposed by third-party payers as well as legislation affecting biopharmaceutical pricing and reimbursement.

For further information:

Corporate Communications

France Nivelle,
Global Communications, UCB
T+32.2.559.9178,
France.nivelle@ucb.com

Jim Baxter,
Neurology Communications, UCB
T+32.2.473.78.85.01,
jim.baxter@ucb.com

Laurent Schots,
Media Relations, UCB
T+32.2.559.92.64,
laurent.schots@ucb.com

Investor Relations

Antje Witte,
Investor Relations, UCB
T+32.2.559.94.14,
antje.witte@ucb.com

Isabelle Ghellynck,
Investor Relations, UCB
T +32.2.559.9588,
isabelle.ghellynck@ucb.com

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