



## UCB's VIMPAT<sup>®</sup> (lacosamide) now approved by FDA to treat partial-onset seizures in pediatric epilepsy patients

- VIMPAT<sup>®</sup> (lacosamide) CV oral formulations are approved as a monotherapy or adjunctive therapy in patients four years of age and older with partial-onset seizures (POS)<sup>1</sup>
- Pediatric epilepsy is the most common, serious, treatable neurological disorder among children and young adults, thought to affect about 470,000 children in the U.S. as of 2015<sup>2,3</sup>
- VIMPAT pediatric approval provides a much-needed new treatment option to support the U.S. pediatric epilepsy community in managing childhood epilepsy, addressing a paucity of medicines approved for this patient population
- Approval builds on existing adult monotherapy and adjunctive therapy indications, broadening clinical application for VIMPAT tablets and oral solution

**Atlanta, Georgia (U.S.) and Brussels (Belgium), 6 November 2017 – 07:00 (CEST):** Today, UCB announced that the U.S. Food and Drug Administration (FDA) has approved a label extension for the company's anti-epileptic drug (AED) VIMPAT<sup>®</sup> (lacosamide) CV as an oral option for the treatment of partial-onset seizures (POS) in pediatric patients four years and older.<sup>1</sup>

This new approval provides clinicians with the option to prescribe VIMPAT to their pediatric patients either as an oral solution or a convenient tablet.<sup>1</sup> This allows for flexible administration options, an important consideration when treating children. As the safety of VIMPAT injection has not been established in pediatric patients, VIMPAT injection is indicated for the treatment of partial-onset seizures only in adult patients (17 years of age and older).<sup>1</sup> Please see additional VIMPAT Important Safety Information below.

The prevalence of pediatric epilepsy has been steadily increasing in the U.S.<sup>4</sup> Today, it is estimated that about 470,000 children in the U.S. under the age of 18 have epilepsy.<sup>2</sup> The U.S. Centers for Disease Control and Prevention (CDC) estimate that 0.6% of children in the U.S. aged 0-17 years have active epilepsy – equivalent to six students in a school of 1000 students.<sup>5</sup> Despite its growing prevalence, approximately 10-20% of pediatric epilepsy patients experience inadequate seizure control with available anti-epileptic drugs.<sup>6,7,8</sup>

*“Although there are many children and families severely affected by epilepsy, until recently there were few effective treatment options approved for childhood epilepsy. This has contributed to poor seizure control for many, which can be detrimental to overall quality-of-life,”* said Dr. Raman Sankar, MD, PhD, Professor of Neurology and Pediatrics and Chief of Pediatric Neurology at the David Geffen School of Medicine at the University of California, Los Angeles. *“The availability of VIMPAT for children with epilepsy has the potential to change the lives of children and their families by providing an additional choice to support them in their epilepsy journey.”*

The expanded FDA indication for 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. Adverse reactions in pediatric patients are similar to those seen in adult patients.<sup>1</sup> This principle of extrapolating clinical data from well controlled studies in adults has been recognized by the FDA as potentially addressing the challenge of limited pediatric data availability.

*“For almost two decades, alongside neurologists, patients and care providers, UCB has worked to progress epilepsy treatment and management, focusing on pioneering research and passion to help improve the lives of people living with epilepsy. We know the impact of living with epilepsy can be especially troubling and complex for children, and that their lives can be significantly compromised by the effects of seizures,”* said Jeff Wren, Executive Vice President, Head of UCB’s Neurology Patient Value Unit. *“The approval of VIMPAT for pediatric use translates our expertise into another real-life potential benefit for children with epilepsy and for the wider pediatric epilepsy community. This is a very proud day for us. With this milestone, we reinforce our commitment to doing everything we can to ensure patients are able to access the right medicines for them at the right time, and to making a real difference for people living with epilepsy - today and for their future.”*

The safety and efficacy profile of VIMPAT as monotherapy and adjunctive therapy for the treatment of POS in adults has been previously established in four multicenter, randomized, controlled clinical trials, each of which met the pre-specified primary endpoints agreed upon with the FDA.<sup>9,10,11,12</sup> UCB also included data from four additional clinical trials within their FDA regulatory submission, along with pharmacokinetic analyses from adult and pediatric data, to support the use of VIMPAT as monotherapy or adjunctive therapy for the treatment of POS in children four years of age and older.<sup>1</sup>

VIMPAT has more than 1,056,500 patient-years of exposure.<sup>13</sup> In the U.S., VIMPAT has been used to treat adult patients with POS since its FDA approval in 2009, providing about 350,000 adult patient exposures.<sup>14</sup>

In the European Union, VIMPAT is also approved as monotherapy and adjunctive therapy in the treatment of POS with or without secondary generalization in adults, adolescents and children from four years of age with epilepsy.<sup>15</sup>

VIMPAT is approved in 72 countries worldwide.

### About VIMPAT in the U.S.

VIMPAT is approved for the treatment of partial-onset seizures in patients 4 years of age and older. As the safety of VIMPAT injection has not been established in pediatric patients, VIMPAT injection is indicated for the treatment of partial-onset seizures only in adult patients (17 years of age and older). VIMPAT was approved in the U.S. in May 2009 as an add-on therapy for adult patients. VIMPAT was approved as monotherapy for adults in August 2014. VIMPAT is available in three formulations: oral tablets, oral solution, and intravenous (IV) injection. Important safety information about VIMPAT in the US is available below.

## IMPORTANT SAFETY INFORMATION

### WARNINGS AND PRECAUTIONS

- **Suicidal Behavior and Ideation:** Antiepileptic drugs (AEDs), including VIMPAT, increase the risk of suicidal behavior and ideation. Monitor patients taking VIMPAT for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Advise patients and caregivers to be alert for these behavioral changes and to immediately report them to the healthcare provider.
- **Dizziness and Ataxia:** VIMPAT may cause dizziness and ataxia. In adult clinical trials, the onset of dizziness and ataxia was most commonly observed during titration. Advise patients not to drive, operate complex machinery, or engage in other hazardous activities until they are familiar with the effects of VIMPAT on their ability to perform such activities. Dizziness and ataxia were also observed in pediatric clinical trials.

- **Cardiac Rhythm and Conduction Abnormalities:**

*PR interval prolongation*

Dose-dependent prolongations in PR interval with VIMPAT have been observed in clinical studies in adult patients and in healthy volunteers. Second-degree and complete AV block have been reported in patients with seizures. When VIMPAT is given with other drugs that prolong the PR interval, further PR prolongation is possible.

Use VIMPAT with caution in patients with known cardiac conduction problems (e.g., marked first-degree AV block, second-degree or higher AV block and sick sinus syndrome without pacemaker), sodium channelopathies (e.g., Brugada Syndrome), or with severe cardiac disease such as myocardial ischemia or heart failure, or structural heart disease. Also, use VIMPAT with caution in patients on concomitant medications that prolong PR interval (e.g., beta-blockers and calcium channel blockers) because of a risk of AV block or bradycardia. In such patients, obtaining an ECG before beginning VIMPAT, and after VIMPAT is titrated to steady-state maintenance dose, is recommended. In addition, closely monitor these patients if they are administered VIMPAT through the intravenous route.

#### *Atrial fibrillation and Atrial flutter*

VIMPAT administration may predispose to atrial arrhythmias (atrial fibrillation or flutter), especially in patients with diabetic neuropathy and/or cardiovascular disease.

- **Syncope:** VIMPAT may cause syncope in adult and pediatric patients.
- **Withdrawal of Antiepileptic Drugs:** Gradually withdraw VIMPAT (over a minimum of 1 week) to minimize the potential of increased seizure frequency.
- **Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS):** Also known as multiorgan hypersensitivity, has been reported with antiepileptic drugs. Some of these events have been fatal or life-threatening. If signs or symptoms are present, immediately evaluate the patient. Discontinue VIMPAT if an alternative etiology for the signs and symptoms cannot be established.
- **Risks in Patients with Phenylketonuria:** VIMPAT oral solution contains aspartame, a source of phenylalanine which can be harmful in patients with phenylketonuria (PKU). A 200 mg dose of VIMPAT oral solution (equivalent to 20 mL) contains 0.32 mg of phenylalanine.

#### **Adverse Reactions**

- **Adjunctive therapy:** In the adult placebo-controlled clinical trials, the most frequently seen adverse reaction with VIMPAT was dizziness (31% vs 8% placebo). Other common adverse reactions occurring in  $\geq 10$  percent of VIMPAT-treated patients, and greater than placebo, were headache, nausea, and diplopia.
- **Monotherapy:** In the adult clinical trial, adverse reactions were generally similar to those observed and attributed to drug in adjunctive placebo-controlled trials, with the exception of

insomnia (occurred at a higher rate of  $\geq 2\%$ ).

- **Pediatric patients:** Adverse reactions reported in clinical studies of pediatric patients 4 to less than 17 years of age were similar to those seen in adult patients.
- **Injection:** In adult adjunctive therapy clinical trials, adverse reactions with intravenous administration generally were similar to those that occurred with the oral formulation, although intravenous administration was associated with local adverse reactions such as injection site pain or discomfort (2.5%), irritation (1%), and erythema (0.5%). When administering a loading dose, the incidence of CNS adverse reactions, such as dizziness, somnolence, and paresthesia may be higher with 15-minute administration than over a 30- to 60-minute period.

### Dosing Considerations

VIMPAT injection is for intravenous and adult use only when oral administration is temporarily not feasible. The loading dose for adult patients should be administered with medical supervision considering the VIMPAT pharmacokinetics and increased incidence of CNS adverse reactions. The safety of VIMPAT injection and the use of a loading dose in pediatric patients have not been studied. Dosage adjustments are recommended for patients with mild or moderate hepatic impairment or severe renal impairment. Use in patients with severe hepatic impairment is not recommended. Perform dose titration with caution in all patients with renal and/or hepatic impairment.

### VIMPAT is a Schedule V controlled substance.

Please refer to full Prescribing Information provided by the sales representative, and visit [www.VIMPATHCP.com](http://www.VIMPATHCP.com).

For more information on VIMPAT<sup>®</sup>, contact 844-599-CARE (2273).

VIMPAT<sup>®</sup> is a registered trademark used under license from Harris FRC Corporation.

### IMPORTANT SAFETY INFORMATION ABOUT VIMPAT<sup>®</sup> IN THE EU AND EEA

VIMPAT<sup>®</sup> 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<sup>®</sup> 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  $\leq$  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  $\leq$  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<sup>®</sup> 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<sup>®</sup> have been observed in clinical studies. Cases with second- and third-degree AV block associated with VIMPAT<sup>®</sup> treatment have been reported in post-marketing experience. VIMPAT<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> may have minor to moderate influence on the ability to drive and use machines. VIMPAT<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> in adult patients with partial-onset seizures who were taking 1-3 concomitant antiepileptic medicinal products. Elevations of ALT to  $\geq 3 \times \text{ULN}$  occurred in 0.7% (7/935) of VIMPAT<sup>®</sup> 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/>.

#### For further information:

##### Communications contacts:

**France Nivelles**, Global Communications, UCB  
T+32.2.559.9178, [france.nivelles@ucb.com](mailto:france.nivelles@ucb.com)

**Jim Baxter**, Neurology Communications, UCB  
T+32.2.473.78.85.01, [jim.baxter@ucb.com](mailto:jim.baxter@ucb.com)

**Laurent Schots**, Media Relations, UCB  
T+32.2.559.92.64, [laurent.schots@ucb.com](mailto:laurent.schots@ucb.com)

##### Investor Relations contacts:

**Antje Witte**, Investor Relations, UCB  
T+32.2.559.94.14, [antje.witte@ucb.com](mailto:antje.witte@ucb.com)

**Isabelle Ghellynck**, Investor Relations UCB  
T+32.2.559.9588, [isabelle.ghellynck@ucb.com](mailto:isabelle.ghellynck@ucb.com)

#### 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](http://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

## 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.

## References

<sup>1</sup> VIMPAT U.S. Prescribing information: Available at <https://www.vimpat.com/vimpat-prescribing-information.pdf>. Accessed November 2017

<sup>2</sup> Shinnar, S., Pellock, J.M. Update on the epidemiology and prognosis of pediatric epilepsy. *J Child Neurol.* 2002;17(Suppl 1):S4-17.

<sup>3</sup> Zack MM, Kobau R. National and State Estimates of the Numbers of Adults and Children with Active Epilepsy — United States, 2015. *MMWR Morb Mortal Wkly Rep* 2017;66:821–825. DOI: <http://dx.doi.org/10.15585/mmwr.mm6631a1>. Accessed October 2017.

<sup>4</sup> Datamonitor Healthcare. *Epilepsy disease coverage*. 2015.

<sup>5</sup> Centers for Disease Control and Prevention. Available at <https://www.cdc.gov/epilepsy/basics/fast-facts.htm>. Accessed November 2017

- 
- <sup>6</sup> Berg AT, Vickrey BG, Testa FM, Levy SR, Shinnar S, DiMario F, et al. How long does it take for epilepsy to become intractable? A prospective investigation. *Ann Neurol*. 2006;60:73-79.
- <sup>7</sup> Berg A, Shinnar S, Levy S, Testa F, Smith-Rapaport S, Beckerman B. Early development of intractable epilepsy in children: a prospective study. *Neurology*. 2001;56:1445-1452.
- <sup>8</sup> Geerts A, Arts WF, Stroink H, Peeters E, Brouwer O, Peters B, et al. Course and outcome of childhood epilepsy: a 15-y follow-up of the Dutch study of epilepsy in childhood. *Epilepsia*. 2010;51:1189-97.
- <sup>9</sup> Chung S, Sperling MR, Biton V, et al; on behalf of the SP754 Study Group. Lacosamide as adjunctive therapy for partial-onset seizures: a randomized controlled trial. *Epilepsia*. 2010;51(6):958-967.
- <sup>10</sup> Halasz P, Kalvianinen R, Mazurkiewicz-Beldzinska M, et al. Adjunctive lacosamide for partial-onset seizures: efficacy and safety results from a randomized controlled trial. *Epilepsia*. 2009;50(3): 443-453.
- <sup>11</sup> Ben-Menachem E, Biton V, Jatuziz D, Abou-Khalil B, Doty P, Rudd GD. Efficacy and safety of oral lacosamide as adjunctive therapy in adults with partial-onset seizures. *Epilepsia*. 2007;48(7):1308-1317.
- <sup>12</sup> Wechsler RT, Li G, French J, et al. Conversion to lacosamide monotherapy in the treatment of focal epilepsy: results from a historical-controlled, multicentre, double-blind study. *Epilepsia*. 2014;55(7):1088-1098
- <sup>13</sup> Periodic Safety Update Report data lock point Dec 15th 2016.
- <sup>14</sup> Data on file (QuintilesIMS National Prescription Audit (NPA), June 2017)
- <sup>15</sup> VIMPAT EU SmPC. Available at [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/EPAR\\_-\\_Product\\_Information/human/000863/WC500050338.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000863/WC500050338.pdf) Accessed November 2017