



UCB reinforces its commitment to epilepsy research with a strong presence at the 2015 American Epilepsy Society annual meeting

- UCB continues a tradition of presenting its latest epilepsy research findings to the American Epilepsy Society.
- 19 presentations, on diverse topics, reinforce how scientific research is underpinning UCB's ongoing commitment to healthcare improvement for patients with epilepsy.

Brussels (Belgium), December 4, 2015 - UCB is pleased to announce that 19 scientific abstracts have been accepted for poster presentation at the upcoming 69th American Epilepsy Society (AES) annual meeting, which takes place from 4th to 8th of December in Philadelphia, PA, USA. The accepted poster presentations¹⁻¹⁹ will cover a range of topics, including three¹⁻³ relating to UCB's approved anti-epileptic drug VIMPAT[®] (lacosamide) C-V, which is approved in the United States as monotherapy or adjunctive therapy for the treatment of partial-onset seizures in people with epilepsy aged 17 years and older.²⁰ In the European Union, VIMPAT[®] is an approved adjunctive therapy for the treatment of partial-onset seizures with or without secondary generalization in adult and adolescent (16-18 years) patients with epilepsy.²¹

Eight presentations⁴⁻¹¹ share recent results from UCB-sponsored and collaborative research, undertaken to evaluate various aspects of epilepsy disorders. Presentations will share findings on aspects including the long-term healthcare costs associated with enzyme inducing antiepileptic drugs vs. non-enzyme active antiepileptic drugs in the UK,⁴ and the characteristics, treatment patterns and outcomes for patients with newly diagnosed epilepsy in the US.^{7,8} Another presentation will share results from a survey of patients' perceptions of healthcare value, showing that perceived treatment value extends beyond direct costs to humanistic healthcare components.⁹ Two presentations will report findings from pre-clinical epilepsy models: One describes a model which could allow early testing of new anti-epileptic compounds or combinations,¹¹ while the other suggests that inflammation may have a role in epileptiform activity.¹⁰ UCB is pleased to announce that the latter poster has also

been accepted for presentation within an Investigator's Workshop; a session highlighting the most outstanding abstracts on topics related to basic science and clinical research.

An additional eight¹²⁻¹⁹ posters will relate to UCB's investigational drug *brivaracetam*, which is currently under review by the FDA and EMA for approval as an adjunctive treatment for partial-onset seizures in adults with epilepsy, but is not currently approved by any regulatory authority worldwide.

UCB's consistent presence at the annual AES meeting demonstrates a continued commitment to sharing its research findings with the epilepsy healthcare community.

"We are once again proud to share our most recent research findings with the AES. UCB has a strong heritage in epilepsy and is committed to driving forward improvements in epilepsy care. Our in-depth research aims to identify and address the unmet needs of patients," said Jeffrey Wren, Head of UCB's Neurology Patient Value Unit. "This year, we are pleased to share the findings from UCB-sponsored and collaborative research covering diverse aspects of epilepsy treatment, including results from pre-clinical testing, international multicenter clinical trials, and responses from patient surveys and database analyses."

The following is a guide to the 19 UCB-sponsored poster presentations at the 69th annual AES meeting, held December 4-8th 2015 in Philadelphia, PA, USA.

Posters will be attended by an author between noon and 2pm on the day of presentation.

Lacosamide posters (3 in total)

- 1. [2.244] Long-term exposure and safety of lacosamide monotherapy for the treatment of partial-onset seizures: results from a multicenter, open-label extension trial**
Vossler D. *et al.*
Sunday 6th December 2015, 8am to 4pm
- 2. [2.251] Efficacy and safety of adjunctive lacosamide for the treatment of partial-onset seizures in Chinese and Japanese adults: a multicenter, double-blind, randomized, placebo-controlled study**
Hong Z. *et al.*
Sunday 6th December 2015, 8am to 4pm
- 3. [3.245] Effects of the antiepileptic drug lacosamide on firing properties and sodium currents in dentate gyrus granule cells of epileptic animals**
Holtkamp D. *et al.*

Monday 7th December 2015, 8am to 2pm

Epilepsy posters (8 in total)

4. [1.203] Long-term healthcare costs in the UK associated with enzyme inducing antiepileptic drugs (EIAEDs) vs non-enzyme active antiepileptic drugs (nEAAEDs)
Borghs S. *et al.*
Saturday 5th December 2015, Noon to 6pm
5. [1.204] Dose-response relationships of AEDs used in refractory epilepsy
Poolos N.P. *et al.*
Saturday 5th December 2015, Noon to 6pm
6. [1.205] Expanded analysis of antiepileptic drug comparative efficacy in refractory epilepsy
Castagna C.E. *et al.*
Saturday 5th December 2015, Noon to 6pm
7. [1.225] Treatment stability in newly diagnosed epilepsy patients: A US database analysis
Thurman D. *et al.*
Saturday 5th December 2015, Noon to 6pm
8. [1.226] Patient characteristics and treatment patterns in newly diagnosed epilepsy patients: a US database analysis
Kalilani L. *et al.*
Saturday 5th December 2015, Noon to 6pm
9. [1.334] Patient perceptions of healthcare value in epilepsy management extend beyond costs to humanistic aspects
Fishman J. *et al.*
Saturday 5th December 2015, Noon to 6pm
10. [3.024] An in vitro hippocampal slice model to probe the role of innate inflammation in epilepsy
Chong S.A. *et al.*
Sunday 6th December 2015, noon to 1.30pm (Investigators' Workshop)

Monday 7th December 2015, 8am to 2pm

11. [3.250] Differentiation of AED classes in a hippocampal slice model of electrically induced ictogenesis

Niespodziany I. *et al.*

Monday 7th December 2015, 8am to 2pm

Brivaracetam posters (8 in total)

12. [1.199] Time from first exposure to discontinuation due to adverse events or lack of efficacy in the brivaracetam clinical program

Elmoufti S. *et al.*

Saturday 5th December 2015, Noon to 6pm

13. [1.219] Evaluation of the pharmacokinetic interaction of brivaracetam on other antiepileptic drugs in adults with partial-onset seizures

Otoul C. and Stockis A.

Saturday 5th December 2015, Noon to 6pm

14. [1.224] Brivaracetam-induced elevation of carbamazepine-epoxide levels: a safety analysis

McDonough B. *et al.*

Saturday 5th December 2015, Noon to 6pm

15. [1.227] Population pharmacokinetics and exposure-response modelling of brivaracetam in adult subjects using daily seizure counts

Stockis A. and Schoemaker R.

Saturday 5th December 2015, Noon to 6pm

16. [1.237] Extrapolation of a brivaracetam exposure-response model from adults to children

Schoemaker R. and Stockis A.

Saturday 5th December 2015, Noon to 6pm

17. [2.253] Efficacy of brivaracetam stratified according to pathological substrate: findings from a Phase 3 clinical trial

Beydoun A. *et al.*

Sunday 6th December 2015, 8am to 4pm

18. [3.253] Efficacy and safety of adjunctive brivaracetam for partial-onset (focal) seizures overall and in elderly patients: a pooled analysis from three Phase 3 studies

Klein P. *et al.*

Monday 7th December 2015, 8am to 2pm

19. [3.261] Efficacy of long-term adjunctive brivaracetam treatment for partial-onset seizures

Johnson M. *et al.*

Monday 7th December 2015, 8am to 2pm

About Epilepsy^{22,23}

Epilepsy is a chronic neurological disorder of the brain. It is the fourth most common neurological condition worldwide and affects approximately 65 million people. In the US, more than 2 million people have epilepsy. Anyone can develop epilepsy; it occurs across all ages, races and genders, and is defined as one or more unprovoked seizures with a risk of further seizures. One third of patients with epilepsy live with uncontrolled seizures.

About UCB in Epilepsy

UCB has a rich heritage in epilepsy with over 20 years of experience in the research and development of antiepileptic drugs. As a company with a long-term commitment to epilepsy research, our goal is to address unmet medical needs. 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 VIMPAT[®] (lacosamide)^{20,21}

VIMPAT[®] is approved in the US as film-coated tablets, injection for intravenous use and oral solution, as monotherapy or adjunctive therapy in the treatment of partial-onset seizures in people with epilepsy ages 17 years and older. VIMPAT[®] injection is indicated as short-term replacement when oral administration is not feasible in these patients.

A single 200 mg loading dose administration option is also approved in the US for all formulations of VIMPAT[®] when used as monotherapy or adjunctive therapy in the treatment of partial-onset seizures in patients with epilepsy aged 17 years and older.

In the European Union, VIMPAT[®] (film-coated tablets, syrup and solution for infusion) is approved 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. VIMPAT[®] is also approved in the European Union for initiation as a single loading dose of 200 mg, followed approximately 12 hours later by a 100 mg twice-daily maintenance dose regimen.

Within Asia, VIMPAT[®] is available in Korea, Hong Kong, Malaysia, Philippines and Thailand. VIMPAT[®] is not approved in Japan and China; regulatory submissions have been completed in 2015.

Important Safety Information about VIMPAT[®] in the US²⁰

Warnings and Precautions

Suicidal Behavior and Ideation: Antiepileptic drugs, 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. The onset of dizziness and ataxia was most commonly observed during titration. Accordingly, patients should be advised 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.

Cardiac Rhythm and Conduction Abnormalities

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

VIMPAT[®] should be used 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. VIMPAT[®] should also be used 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, is recommended. In addition, these patients should be closely monitored 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.

Withdrawal of Antiepileptic Drugs: VIMPAT[®] should be gradually withdrawn (over a minimum of 1 week) to minimize the potential of increased seizure frequency.

Multiorgan Hypersensitivity Reactions: Multiorgan hypersensitivity reactions (also known as Drug Reaction with Eosinophilia and Systemic Symptoms, or DRESS) have been reported with antiepileptic drugs. If this reaction is suspected, VIMPAT[®] should be discontinued and alternative treatment started.

Phenylketonurics: VIMPAT[®] oral solution contains aspartame, a source of phenylalanine. A 200 mg dose of VIMPAT[®] oral solution (equivalent to 20 mL) contains 0.32 mg of phenylalanine.

Adverse Reactions

Adjunctive therapy: In the placebo controlled clinical trials, the most frequently seen adverse reaction with VIMPAT[®] was dizziness (31% vs 8% placebo). Other common adverse reactions occurring in ≥ 10 percent of VIMPAT-treated patients, and greater than placebo, were headache, nausea, and diplopia.

Monotherapy: In the clinical trial, adverse reactions were generally similar to those observed and attributed to drug in adjunctive placebo controlled trials, with the exception of insomnia (observed at a higher rate of $\geq 2\%$).

Injection: In adjunctive therapy clinical trials, adverse reactions with intravenous administration generally were similar to those observed with the oral formulation, although intravenous administration was associated with local adverse events 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

The loading dose should be administered with medical supervision considering the VIMPAT[®] pharmacokinetics and increased incidence of CNS adverse reactions. 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. Dose titration should be performed 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 at <http://www.vimpat.com/hcp>.

For more information on VIMPAT[®] contact 844-599-CARE (2273).

VIMPAT[®] is a registered trademark used under license from Harris FRC Corporation.

Important Safety Information about VIMPAT[®] in the EU and EEA²¹

VIMPAT[®] (lacosamide) 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 intravenous 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 central nervous system 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 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 behavior have been reported in patients treated with anti-epileptic agents in several indications. Therefore patients should be monitored for signs of suicidal ideation and behaviors and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behavior 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.

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.

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 central nervous system and gastrointestinal adverse reactions usually decreased over time. Incidence of central nervous system 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 $\geq 3 \times \text{ULN}$ occurred in 0.7% (7/935) of VIMPAT® patients and 0% (0/356) of placebo patients. 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: 6th February 2015.

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000863/WC500050338.pdf. (Accessed 12th November 2015)

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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 8500 people in about 40 countries, the company generated revenue of EUR 3.3 billion in 2014. 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.

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