



**FOR THE ATTENTION OF ACCREDITED MEDICAL WRITERS**

## **New analysis of pooled clinical data showed VIMPAT<sup>®</sup> (lacosamide) significantly improved partial-onset seizure control, increased seizure freedom rates and enhanced patient function**

**Brussels, BELGIUM 29th June 0900CET** – New pooled clinical data presented at the 28th International Epilepsy Congress (IEC) in Budapest, Hungary showed that VIMPAT<sup>®</sup> (lacosamide), a new antiepileptic drug (AED) with a novel mode of action,<sup>1,2</sup> significantly improved seizure control, increased seizure freedom rates during the maintenance phase and enhanced quality of life and patient function, when used as adjunctive therapy in adult patients with uncontrolled partial-onset seizures.<sup>2,3</sup>

A pooled analysis of all doses from three similarly designed Phase II/III trials showed that lacosamide (200 mg, 400 mg, 600\* mg/day) significantly reduced partial-onset seizures, compared to placebo ( $p < 0.05$ ), when administered with 1-3 AEDs<sup>1,3,5</sup>

Lacosamide provided a dose-dependent increase in efficacy for primary endpoints (partial onset seizure frequency and 50% responder rates) at all doses\* studied, and for 75% responder rates up to 400 mg/day as a secondary endpoint.<sup>3,5</sup>

Patients responding to lacosamide (200 mg, 400 mg, 600\* mg/day) reported improvements in health status, quality of life and patient function.<sup>4,5</sup>

“Sixty percent of people living with epilepsy have partial-onset seizures and around one third remain uncontrolled, despite trying treatment with a range of antiepileptic drugs. These studies supported the effectiveness of lacosamide in reducing partial-onset seizures and improving seizure control when added to existing antiepileptic drug regimens in a population where most patients were uncontrolled on two-three AEDs,” said Professor Elinor Ben-Menachem, Professor of Neurology and Epilepsy and Clinical Trial Investigator, Institute of Clinical Neurosciences, Goteborg University, Sweden.

In Europe, VIMPAT<sup>®</sup> is indicated as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in patients with epilepsy aged 16 years and over.<sup>1</sup> In the U.S. VIMPAT<sup>®</sup> is indicated as adjunctive therapy in the treatment of partial-onset seizures in patients with epilepsy aged 17 years and older.<sup>6</sup> It is a Schedule V controlled substance in the U.S.



## **Summary of Lacosamide Data Presented at the 2009 IEC Congress, Budapest, Hungary**

### **Adjunctive lacosamide significantly reduced partial-onset seizures at all doses\* studied<sup>3</sup>**

A pooled analysis of three Phase II/III trials showed that lacosamide significantly reduced partial-onset seizures compared with placebo at all doses studied (200, 400, 600\* mg/day).

Lacosamide (400 and 600\* mg) significantly reduced partial-onset seizure frequency and improved 50% responder rates compared to placebo in all individual studies ( $p < 0.05$  for all analyses).

To further evaluate 200 mg/day lacosamide, a meta-analysis was conducted that showed a significant difference from placebo for both primary efficacy endpoints ( $p < 0.05$ ).

The pooled analysis comprised 1,294 subjects randomised to lacosamide (200 mg/day,  $n=267$ ; 400 mg/day,  $n=466$ ; 600\* mg/day,  $n = 202$ ) and 359 randomised to placebo, who had at least one post-baseline efficacy assessment.

### **Adjunctive lacosamide improved seizure freedom rates and $\geq 75\%$ responder rates with increasing dose\*<sup>5</sup>**

Pooled analysis from Phase II/III clinical trials showed a dose-responsive trend for seizure freedom rates with an increasing dose\* of lacosamide (2.7%, 3.3% and 4.8% for 200, 400 or 600\* mg/day vs 0.9% placebo) in a patient population predicted to have a poor response to treatment.

Seizure freedom was defined as the proportion of enrolled patients who completed the study and remained seizure free throughout a 12-week maintenance period.

The percentage of patients experiencing a 75% or greater reduction in partial-onset seizure frequency from the baseline to maintenance period was also evaluated.

A dose response was evident in 75% responder rates between lacosamide 200 and 400 mg/day. Increasing the dose to 600\* mg/day did not increase the response, possibly due to the fixed-dose trial design, combined with lower tolerability observed at doses of lacosamide above 400mg/day.

### **Patients who responded to lacosamide showed improvements across all measured areas of patient functioning<sup>4</sup>**

A pooled analysis from three Phase II/III trials evaluating lacosamide (200, 400 or 600\* mg/day) showed patients responding to lacosamide experienced self-reported improvements in quality of life, patient function and health status.

In patients stratified by treatment group and level of clinical response the impact of lacosamide on patient's lives was assessed via secondary endpoints including mean Quality of Life Inventory In Epilepsy (QOLIE-31) and Seizure Severity Scale (SSS) score changes from baseline, and distribution of Patient Global Impression of Change (PGIC) (Phase III trials only) at last assessment.



Responders with more than 50% seizure reduction in the overall patient population and lacosamide treatment groups experienced significant improvements in QOLIE-31 and SSS scores from baseline ( $p < 0.05$  for all comparisons of responders to non-responders). Largest improvements were obtained for quality of life score including QOLIE-31 seizure worry and social functioning, as well as SSS overall score. For the PGIC analysis more than 80% of lacosamide responders reported an improved health status.

The QOLIE-31 analysis comprised 1,046 patients including 738 subjects randomised to lacosamide (PGIC: 829 total including 575 lacosamide; SSS: 823 total including 571 lacosamide).

### **Adjunctive lacosamide was generally well-tolerated when combined with up to three concomitant AEDs<sup>7</sup>**

A pooled analysis of data from three Phase II/III trials, comprising 944 subjects randomised to lacosamide, showed that lacosamide was generally well-tolerated compared with placebo, when combined with 2-3 concomitant AEDs.

The most commonly reported treatment-emergent adverse events, in  $\geq 10\%$  of the lacosamide group and greater than placebo, were dizziness (31% vs. 8%), headache (13% vs. 9%), nausea (11% vs. 4%) and diplopia (11% vs. 2%).<sup>6</sup>

Most adverse events were mild to moderate in intensity and some were dose-related<sup>1</sup>.

*\*The recommended maintenance dose of lacosamide is 200 mg to 400 mg/day. The 600 mg/day dose of lacosamide is not approved by the EMEA and FDA. In clinical trials, the overall efficacy of the 600 mg/day dose was similar to the 400 mg daily dose, and was associated with a higher rate of CNS and gastrointestinal-related adverse reactions.<sup>1,6</sup>*

### **Lacosamide clinical trials program**

Analyses of pooled data from one phase II and two phase III double-blind, placebo-controlled trials, evaluated the efficacy and safety of lacosamide (200 mg, 400 mg and 600\* mg/day) as adjunctive therapy in more than 1,308 adults with uncontrolled partial-onset seizures with or without secondary generalisation.<sup>1,3</sup> Seizure reduction was measured by the primary endpoints: median percent reduction in seizure frequency per 28 days from baseline to maintenance period; and the 50% responder rate, defined as the proportion of patients experiencing a 50% or greater reduction in partial-onset seizure frequency per 28 days from baseline to the maintenance period.<sup>3</sup>

At baseline, most patients (85%) were uncontrolled on 2-3 AEDs, and had high seizure frequencies which are predictors for a poor response to treatment.<sup>7,8,9,10,</sup>

### **Important safety information about VIMPAT<sup>®</sup> in Europe<sup>1</sup>**

VIMPAT<sup>®</sup> is indicated as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in patients with epilepsy aged 16 years and older. VIMPAT<sup>®</sup> solution for infusion is an alternative for patients when oral administration is temporarily not feasible. Contraindications: Hypersensitivity to the active substance or to peanuts or soya or to any of the excipients; known second- or third-degree atrioventricular (AV) block. Special warnings and precautions for use: Treatment with lacosamide 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 lacosamide have been observed in clinical studies. Lacosamide 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 lacosamide is used in combination with products known to be associated with PR prolongation. Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic agents. 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. Undesirable effects: The most common adverse reactions (>10%) are dizziness, headache, diplopia, and nausea. Other common adverse reactions (1-10%) are depression, balance disorder, coordination abnormal, memory impairment, cognitive disorder, somnolence, tremor, nystagmus, vision blurred, vertigo, vomiting, constipation, flatulence, pruritus, gait disturbance, asthenia, fatigue, fall, and skin laceration. Refer to the European Summary of Product Characteristics for full prescribing information.

<http://www.emea.europa.eu/humandocs/PDFs/EPAR/vimpat/H-863-PI-en.pdf> (Accessed 02 March 2009)<sup>1</sup>

**Important safety information about Vimpat® in the U.S.**

Vimpat® (lacosamide C-V) is a medicine that is used with other medicines to treat partial onset seizures in patients 17 years of age and older with epilepsy. Vimpat® is generally well-tolerated, but may not be for everyone. Patients should discuss with their doctor if Vimpat® is right for them.

The most common side effects with Vimpat® are dizziness, headache, nausea and double vision. Vimpat® may also cause problems with coordination and balance. Patients should not drive, operate machinery or do other dangerous activities until they know how Vimpat® affects them. Patients should not stop taking Vimpat® without first talking to their doctor. Stopping Vimpat® suddenly can cause serious problems. Vimpat® could make patients feel faint. Patients should tell their doctor if they have a heart condition or if they are taking other medicines that affect the heart. In rare cases, Vimpat® may cause reactions that could affect the heart, liver or kidney. The patient should contact their doctor immediately if they are tired, have jaundice (yellowing of skin or eyes), and have dark urine. Antiepileptic drugs, including Vimpat®, may cause suicidal thoughts or actions in a very small number of people, about 1 in 500. Patients should call their healthcare provider right away if they have new or worsening symptoms of depression, any unusual changes in mood or behavior, or suicidal thoughts, behavior, or thoughts about self harm that they have never had before or may be worse than before. To report SUSPECTED ADVERSE REACTIONS, contact UCB, Inc. at 866-822-0068 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

Please see additional patient information including the Vimpat® Medication Guide at the end of the full prescribing information on [www.Vimpat.com](http://www.Vimpat.com)

***For further information***

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1. *VIMPAT<sup>®</sup> Summary of Product Characteristics*
2. *Beyreuther BK, Freitag J, Heers C et al. Lacosamide: A Review of Preclinical Properties. CNS Drug Reviews 2007; 13: 21-42*
3. *Ben-Menachem E, Chung S, Rudd D, Hebert D and Doty P. Evaluation of Lacosamide Efficacy in Subjects with Partial-Onset Seizures Across the Dose Range Used in Phase II/III Clinical Trials. Poster Presentation, 28<sup>th</sup> International Epilepsy Congress 28 June – 2 July 2009*
4. *De La Loge, C, Cramer J, Borghs S, Mueller K, Eggert A, Doty P. Improvement in patient-reported outcomes seen in patients responding to lacosamide: Pooled QOLIE-31, SSS and PGIC data from 3 Phase II/III clinical trials. Poster Presentation, 28<sup>th</sup> International Epilepsy Congress 28 June – 2 July 2009*
5. *French J, Brodie M, Hebert D, Isojarvi J, Doty P. Evaluation of Seizure Freedom and 75% Responder Rates with Lacosamide in Subjects with Partial-Onset Seizures in Phase II/III Clinical Trials. Poster Presentation, 28<sup>th</sup> International Epilepsy Congress 28 June – 2 July 2009*
6. *VIMPAT<sup>®</sup> Prescribing Information (US)*
7. *Gil-Nagel A, Biton V, Fountain N, Rosenow F, Hebert D, Doty P. The Safety and Tolerability of Lacosamide in Randomized, Double-Blind, Placebo-Controlled Phase II/III Trials. Poster Presentation, 28<sup>th</sup> International Epilepsy Congress 28 June – 2 July 2009*
8. *Ben-Menachem E, et al. Efficacy and Safety of Oral Lacosamide for the Treatment of Partial Onset Seizures as Adjunctive Therapy in Adults with Partial Onset Seizures. Epilepsia 2007;48(7):1308-1317*
9. *Callaghan BC, Anand K, Hesdorffer D, Hauser WA, French JA. Likelihood of seizure remission in an adult population with refractory epilepsy. Ann Neurol 2007; 62(4) 382-389*
10. *Hitiris N et al Predictors of pharmaco-resistant epilepsy. Epilepsy Research 2007; 75: 192-196*

#### **About UCB**

UCB, Brussels, Belgium ([www.ucb.com](http://www.ucb.com)) is a biopharmaceutical company dedicated to the research, development and commercialization of innovative medicines with a focus on the fields of central nervous system and immunology disorders. Employing more than 10 000 people in over 40 countries, UCB achieved revenue of 3.6 billion euro in 2008. UCB is listed on Euronext Brussels (symbol: UCB).

#### **Forward looking statement**

*This press release contains forward-looking statements based on current plans, estimates and beliefs of management. Such statements are subject to risks and uncertainties that may cause actual results to be materially different 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, effects of future judicial decisions, changes in regulation, exchange rate fluctuations and hiring and retention of its employees.*