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# *Press Release*

## CHMP Adopts Positive Opinion Recommending Approval of Keppra® as Adjunctive Therapy in the Treatment of Primary Generalised Tonic-Clonic Seizures

**Brussels, Belgium, 23 November 2006 – 7:00am CET**: UCB today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMEA) had issued a positive opinion recommending that the European Commission grant a marketing authorisation for Keppra® (levetiracetam) as adjunctive therapy in the treatment of primary generalised tonic-clonic (PGTC) seizures in adults and adolescents from 12 years of age with Idiopathic Generalised Epilepsy (IGE).

Keppra® is already licensed in the European Union as[2]:

- Monotherapy in the treatment of partial onset seizures with or without secondary generalisation in patients from 16 years of age with newly diagnosed epilepsy
- Adjunctive therapy for partial onset seizures with or without secondary generalisation in adults and children from 4 years of age with epilepsy
- Adjunctive therapy for myoclonic seizures in adults and adolescents from 12 years of age with Juvenile Myoclonic Epilepsy (JME)

*'The CHMP recommendation represents another important milestone in the development program for Keppra®. In the clinical trial supporting this application, Keppra® was well tolerated and significantly reduced tonic-clonic seizures. We now look forward to the determination of the European Commission, and hopefully making Keppra® available to more patients with generalised seizures.'* said Troy Cox, President CNS Operations, UCB.

## Key Study Results[1]

The efficacy and tolerability of adjunctive Keppra® treatment was examined in a double-blind, placebo controlled study which included adults, adolescents and a limited number of children (the intent-to-treat population consisted of 163 patients age range 4-65 years) suffering from IGE with uncontrolled PGTC seizures in different syndromes, despite baseline treatment with one-two other antiepileptic drugs. In the study patients were randomised to either Keppra® (3000 mg/day for adults and adolescents or 60 mg/kg/day for children), or placebo. A four-week double blind period of up-titration was followed by a 20-week stable dose period[1].

***Seizure freedom:*** during the stable dose period, 34.2% of those who took Keppra® were free from PGTC seizures compared with 10.7% of those in the placebo group (*p<0.001*).

***Seizure frequency****:* during the total treatment period, 72.2% of patients achieved at least a 50% reduction of PGTC seizure frequency per week, compared to 45.2% of placebo patients (*p=0.0005*).

***Safety:*** an assessment of safety data showed similar findings to the established tolerability profile of Keppra®. The most commonly reported undesirable effect was fatigue. During the double-blind period, 1.3% of Keppra® patients and 4.8% of placebo patients withdrew due to adverse events.

## About Idiopathic Generalised Epilepsy and Primary Generalised Tonic-Clonic Seizures

Idiopathic generalised epilepsies (IGE) are a range of generalised epilepsies for which there is no obvious cause, other than an inherited (genetic) predisposition. They are characterised by generalised tonic-clonic, absence and myoclonic seizures. Tonic- clonic seizures can be the most debilitating seizures type within the category of IGE[4]. These seizures begin with a sudden loss of consciousness and stiffening of the muscles, followed by rapid rhythmic jerking of the arms and legs. Other symptoms such as a change in heart rate and blood pressure, increased production of saliva and an increase in bladder pressure that often causes incontinence can also occur[4]. Epidemiological studies indicate that these generalised tonic-clonic seizures are common with their incidence estimated at 23% of all cases of epilepsy[5].

**About Keppra® in Europe[2]**

Keppra® is indicated as monotherapy in the treatment of partial onset seizures with or without secondary generalisation in patients from 16 years of age with newly diagnosed epilepsy; as adjunctive therapy in the treatment of partial onset seizures with or without secondary generalisation in adults and children from 4 years of age with epilepsy; and as adjunctive therapy in the treatment of myoclonic seizures in adults and adolescents from 12 years of age with JME. In monotherapy the most commonly reported side effects were fatigue and somnolence. As adjunctive therapy in adults with partial onset seizures the most commonly reported side effects were somnolence, asthenia and dizziness. As adjunctive therapy in paediatric patients (4-16 years of age) with partial onset seizures the most commonly reported side effects were somnolence, hostility, nervousness, emotional lability, agitation, anorexia, asthenia and headache. In adults and adolescents with myoclonic seizures the most common reported side effects associated with Keppra® in combination with other AEDs were headache and somnolence. Keppra® is also indicated for intravenous administration and is available as 100 mg/ml concentrate for solution for infusion. The most common adverse events from Keppra® intravenous use were dizziness, somnolence, headache and postural dizziness. Please consult local prescribing information.

**About Keppra® in the US[3]**

Keppra® is indicated as adjunctive therapy in the treatment of partial onset seizures in adults and children 4 years of age and older with epilepsy and as adjunctive therapy in the treatment of myoclonic seizures in adults and adolescents 12 years of age and older with juvenile myoclonic epilepsy. Keppra® is associated with the occurrence of central nervous system adverse events including somnolence and fatigue and behavioral abnormalities, as well as hematological abnormalities. In adults experiencing partial onset seizures, Keppra® is also associated with coordination difficulties. In pediatric patients 4-16 years of age experiencing partial onset seizures, the most common adverse events associated with Keppra® in combination with other antiepileptic drugs (AEDs) were somnolence, accidental injury, hostility, nervousness and asthenia. In adults experiencing partial onset seizures, the most common adverse events associated with Keppra® in combination with other AEDs were somnolence, asthenia, infection and dizziness. In adults and adolescents 12 years of age and older with juvenile myoclonic epilepsy, the most common adverse events associated with Keppra® in combination with other AEDs were somnolence, neck pain and pharyngitis. Keppra® is also available as an intravenous formulation for the adjunctive treatment of partial-onset seizures in adults with epilepsy. Keppra® injection is an alternative for patients when oral administration is temporarily not feasible. The adverse events that may result from Keppra® injection use for partial onset seizures include all those associated with Keppra® tablets and oral solution. For the U.S., prescribing information is available at www.keppra.com.

**About UCB**

UCB (www.ucb-group.com) is a leading global biopharmaceutical company dedicated to the research, development and commercialisation of innovative pharmaceutical and biotechnology products in the fields of central nervous system disorders, allergy/respiratory diseases, immune and inflammatory disorders and oncology – UCB focuses on securing a leading position in severe disease categories. Employing over 8,300 people in over 40 countries, UCB achieved revenue of 2.3 billion euro in 2005. UCB is listed on the Euronext Brussels Exchange. Worldwide headquarters are located in Brussels, Belgium.

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**References**

1. Rosenfeld WE, Berkovic S, Knowlton R on behalf of Lev N01057 PGTC Study Group. Efficacy and safety of levetiracetam as adjunctive treatment in adult and paediatric patients suffering from idiopathic generalized epilepsy with primary generalized tonic-clonic seizures. [abstract]. Neurology 2006; 66 (5 Suppl 2): A40

2. Summary of Product Characteristics

3. U.S. Full Prescribing Information Keppra® tablets and oral solution Rev 23E 10/2006 and Keppra® injection Rev 2E 10/2006 (available at www.Keppra.com)

4. www.epilepsy.com/epilepsy/seizures_tonicclonic (accessed 20th November 2006)

5. Hauser, W.A., Annegers, J.F. & Kurland, L.T. (1993) Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935-1984 Epilepsia, 34 (3), 453-468