UCB News

UCB receives CHMP positive opinion for adjunctive use of BRIVIACT® as paediatric treatment for epilepsy patients

- CHMP positive opinion for BRIVIACT® (brivaracetam) extends therapeutic indication to include adjunctive therapy in the treatment of partial onset seizures with or without secondary generalisation in patients with epilepsy from 4 years of age.[1]
- Epilepsy is the most common serious neurological disorder among children and young adults with a prevalence in Europe ranging from 3.2 – 5.1 per 1,000.[2]
- Despite this high prevalence, approximately 10 – 29% of paediatric epilepsy patients experience inadequate seizure control with currently available anti-epileptic drugs.[3,4]

Brussels (Belgium), 1st June 2018 – 18:00 (CEST): UCB has today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion for BRIVIACT® (brivaracetam) to extend the therapeutic indication to include adjunctive therapy in the treatment of partial onset seizures with or without secondary generalisation in patients with epilepsy from 4 years of age.

The European Commission is expected to make a decision based on this CHMP positive opinion over the coming weeks . When approved, BRIVIACT's paediatric indication will represent an important new treatment option for children with epilepsy, their family and care-givers, as well as European healthcare professionals.

BRIVIACT is the newest medicine in the family of the synaptic vesicle protein 2A (SV2A) anti-epileptic drugs (AED) – a class of medicines discovered and developed by UCB. BRIVIACT

demonstrates a high and selective affinity for SV2A in the brain which may contribute to its anticonvulsant effects.

"We're very proud to be at the forefront of global epilepsy management, and to be able to provide healthcare professionals, their patients and their family members with new and additional choices to support them in their individual epilepsy journeys." said Jeff Wren, Executive Vice-President, Head of UCB's Neurology Patient Value Unit. *"Today's positive CHMP opinion for BRIVIACT® is another important step forwards in our efforts to realize true patient value and to further improve the lives of this highly impacted patient population by providing additional treatment options."*

Epilepsy is a chronic neurological disorder, affecting approximately 65 million people worldwide.[5] It is the most common serious neurological disorder among children and young adults,[6] with a prevalence amongst children in Europe ranging from 3.2 – 5.1 per 1,000.[2]

The stigma associated with epilepsy, especially during adolescence, has been related to low self-esteem, worry, and negative feelings about life,[7] with 12 – 26% of children with epilepsy reporting depression and anxiety.[8] Paediatric patients may suffer from side effects with currently available AEDs.[9] As such, there is a need for additional treatment options that may provide seizure control with a low side effect profile.

The CHMP positive opinion for the use of BRIVIACT in paediatric patients 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. This principle of extrapolating clinical data from well controlled studies in adults has been recognized by the EMA as potentially addressing the challenge of limited paediatric data availability. As a result, proven AEDs, which have previously been approved for treating adults with epilepsy, are becoming available to paediatric epilepsy patients for the first time. This brings massive potential to improve the management of seizures for paediatric patients. UCB has embraced these guidelines, addressing a significant need for this previously poorly served patient population.

About BRIVIACT®

BRIVIACT (brivaracetam) is a new molecular entity that was rationally designed and developed by UCB. Brivaracetam displays a high and selective affinity for synaptic vesicle protein 2A (SV2A) in the brain, which may contribute to the anticonvulsant effect. However, the precise mechanism of action by which BRIVIACT exerts its anticonvulsant activity is not known.

In the European Union, BRIVIACT is currently indicated as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adult and adolescent patients from 16 years of age with epilepsy.[10]

In the U.S., BRIVIACT CV is indicated for the treatment of partial-onset seizures in patients 4 years of age and older.[11]

About Epilepsy[5,12,13,14]

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. Around one third of patients with epilepsy currently live with uncontrolled seizures.

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 in immunology or neurology. With more than 7 500 people in approximately 40 countries, the company generated revenue of € 4.5 billion in 2017. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news

Important Safety Information about BRIVIACT® in the EU and EEA
BRIVIACT® (brivaracetam) is indicated as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adult and adolescent patients from 16 years of age with epilepsy. **Contraindications** Hypersensitivity to the active substance, other pyrrolidone derivatives or any of the excipients. **Special warnings and precautions for use** Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic drugs (AEDs) in several indications, including BRIVIACT®. Patients should be monitored for signs of suicidal ideation and behaviour and appropriate treatment should be considered. Patients (and caregivers) should be advised to seek medical advice should any signs of suicidal ideation or behaviour emerge. Dose adjustments are recommended for patients with hepatic impairment (50 mg/day starting dose should be considered, up to maximum daily dose of 150 mg administered in 2 divided doses). BRIVIACT® film-coated tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take BRIVIACT®. Both the solution for injection/infusion and the oral solution contain sodium – to be taken into consideration for patients on a controlled sodium diet. The oral solution contains sorbitol (E420). Patients with rare hereditary problems of fructose intolerance should not take this medicine. The oral solution contains methyl parahydroxybenzoate (E218), which may cause allergic reactions (possibly delayed). **Interaction with other medicinal products and other forms of interaction** With co-administration of BRIVIACT® 200 mg single dose and ethanol 0.6 g/L continuous infusion in healthy subjects there was no pharmacokinetic interaction, but the effect of alcohol on psychomotor function, attention and memory was doubled. Intake of BRIVIACT® with alcohol is not recommended. In healthy subjects, co-administration with rifampicin, a strong enzyme-inducer (600 mg/day for 5 days), decreased BRIVIACT® area under the plasma concentration curve (AUC) by 45%. Prescribers should consider adjusting the dose of BRIVIACT® for patients starting or ending treatment with rifampicin. Other strong enzyme-inducers (such as St

John´s wort [Hypericum perforatum]) may also decrease the systemic exposure of BRIVIACT®. Therefore, starting or ending treatment with St John's wort should be done with caution. In vitro interaction studies have shown that BRIVIACT® can inhibit CYP2C19, therefore BRIVIACT® may increase plasma concentrations of medicinal products metabolised by CYP2C19 (e.g., lanzoprazole, omeprazole, diazepam). CYP2B6 induction has not been investigated in vivo and BRIVIACT® may decrease plasma concentrations of medicinal products metabolised by CYP2B6 (e.g. efavirenz). In vitro studies have also shown that BRIVIACT® has inhibitory effects on OAT3. BRIVIACT® 200 mg/day may increase plasma concentrations of medicinal products transported by OAT3. BRIVIACT® plasma concentrations are decreased when co-administered with strong enzyme inducing antiepileptic drugs (carbamazepine, phenobarbital, phenytoin) but no dose adjustment is required. **Effects on ability to drive and use machines** BRIVIACT®, has minor or moderate influence on the ability to drive and use machines. Patients should be advised not to drive a car or to operate other potentially hazardous machines until they are familiar with the effects of BRIVIACT®, on their ability to perform such activities. **Undesirable effects** The most frequently reported adverse reactions with BRIVIACT® (reported by >10% of patients) were somnolence (14.3%) and dizziness (11.0%). They were usually mild to moderate in intensity. Somnolence and fatigue (8.2 %) were reported at higher incidences with increasing dose. Other common adverse reactions (≥1% to <10%) were influenza, decreased appetite, depression, anxiety, insomnia, irritability, convulsion, vertigo, upper respiratory tract infections, cough, nausea, vomiting and constipation. Neutropenia has been reported in 0.5% (6/1,099) BRIVIACT® - patients and 0% (0/459) placebo-treated patients. Four of these patients had decreased neutrophil counts at baseline, and experienced additional decrease in neutrophil counts after initiation of BRIVIACT®. None of the six cases were severe, required any specific treatment, led to BRIVIACT® discontinuation or had associated infections. Suicidal ideation was reported in 0.3 % (3/1099) of BRIVIACT® -treated patients and 0.7 % (3/459) of placebo-treated patients. In short-term clinical studies of BRIVIACT® in patients with epilepsy, there were no cases of completed suicide and suicide attempt, however both were reported in the long-term open-label extension studies. In patients who were followed up in the open-label extension studies for up to 8 years, the safety profile was similar to that observed in the short-term, placebo-controlled studies. Reactions suggestive of immediate (Type I) hypersensitivity have been reported in a small number of BRIVIACT® patients (9/3022) during clinical development. **Overdose** There is limited clinical experience with BRIVIACT® overdose in humans. Somnolence and dizziness were reported in a healthy subject taking a single dose of 1,400 mg of BRIVIACT® . There is no specific antidote. Treatment of an overdose should include general supportive measures. Since less than 10% of BRIVIACT® is excreted in urine, haemodialysis is not expected to significantly enhance BRIVIACT® clearance.

Refer to the European Summary of Product Characteristics for other adverse reactions and full prescribing information. Date of revision: 21 April 2017.

http://www.ema.europa.eu/

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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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