



UCB
News

UCB announces BRIVIACT[®] (brivaracetam) now approved by FDA to treat partial-onset (focal) seizures in pediatric epilepsy patients

- BRIVIACT[®] (brivaracetam) CV oral formulations are approved as a monotherapy or adjunctive therapy in patients four years of age and older with partial-onset seizures.
- Approval provides pediatric epilepsy patients a treatment option which can be initiated at a therapeutic dose from day one.
- Pediatric epilepsy is the most common, serious neurological disorder among children and young adults, thought to affect nearly 470,000 children in the U.S.^{1,2}
- Indication comes less than 2 years after the launch of BRIVIACT in the U.S., building on existing adult monotherapy and adjunctive therapy indications, and broadening clinical application for UCB's newest anti-epilepsy drug.

Atlanta, Georgia (U.S.) & Brussels (Belgium), 0700 CEST, 14 May, 2018: UCB announced today that the U.S. Food and Drug Administration (FDA) has approved a supplemental new drug application (sNDA) for the company's newest anti-epileptic drug (AED) BRIVIACT[®] (brivaracetam) CV oral formulations indicated as monotherapy and adjunctive therapy in the treatment of partial onset (focal) seizures in patients age four years and older.

This approval provides clinicians with the convenient option to prescribe BRIVIACT to their pediatric patients as a tablet or oral solution, providing flexible administration options which are important considerations when treating children.

As the safety of BRIVIACT injection has not been established in pediatric patients, BRIVIACT injection is indicated for the treatment of partial-onset seizures only in patients 16 years of age and older. Please see additional BRIVIACT Important Safety Information below.

As a result of the FDA's decision, children age four years and older with partial-onset seizures in the U.S. can now be treated with BRIVIACT. This extends the clinical application for BRIVIACT which already has a similar indication for adults.

BRIVIACT is the newest anti-epileptic drug (AED) in the synaptic vesicle protein 2A (SV2A) family of medicines – a class of medicines discovered and developed by UCB. BRIVIACT demonstrates a high and selective affinity for SV2A in the brain. It is highly permeable and is rapidly and almost completely absorbed which may contribute to its anticonvulsant effects. Gradual dose escalation is not required when initiating treatment with BRIVIACT for monotherapy or adjunctive therapy, allowing clinicians to initiate treatment at a therapeutic dose from day one.

“As a pediatric neurologist, one of the most challenging aspects in treating epilepsy in children is establishing, quickly, which anti-epilepsy drug will support them best in managing their seizures. The impact of poor seizure control can be extremely detrimental – both to overall quality of life for patients and caregivers and for a child’s development. There is a real sense of urgency for parents and healthcare providers to know whether a particular therapeutic approach is likely to be successful, minimizing some of the challenges associated with epilepsy and potentially allowing them to live a normal and active life,” explained Dr. James Wheless, Director, Neuroscience Institute & Le Bonheur Comprehensive Epilepsy Program - Le Bonheur Children’s Hospital. *“The availability of an approved treatment option, such as BRIVIACT, has potential to help improve the lives of children and their families by providing an additional choice to support them in their epilepsy journey.”*

Epilepsy in childhood is a complex disorder that can have a significant impact on many aspects of a child's development and function. Social and societal stigma still associated with epilepsy can be especially cruel for children. The prevalence of pediatric epilepsy has been steadily increasing in the U.S.³ Today, it is estimated that nearly 470,000 children in the U.S. under the age of 18 have epilepsy, representing around a quarter of the total worldwide population who develop the condition each year.⁴ The U.S. Centers for Disease Control and Prevention (CDC) estimate that 0.6 percent of children in the U.S. ages 0 to 17 have active epilepsy – equivalent to six students in a school of 1000.⁵ Despite its growing prevalence, approximately 10 to 20 percent of pediatric epilepsy patients experience inadequate seizure control with available anti-epileptic drugs.^{6,7,8} Alongside close partnerships with educators, family members, and healthcare providers, there is a need for newer AEDs with better seizure control which can support and maximize a child’s potential for academic success.

“We believe there is a real need for newer AEDs to support and maximize the potential for success for children with epilepsy,” explained Jeff Wren, Executive Vice-President, Head of UCB’s Neurology Patient Value Unit. “The approval of BRIVIACT in the U.S for pediatric patients represents an important milestone for patients, families, doctors, UCB, and the wider epilepsy community, and has the potential to provide additional value for patients - both today and for their future. We are very excited to be able to provide a new pediatric treatment choice, and we are proud to support patients as they progress on their epilepsy journey.”

The expanded FDA indication for BRIVIACT 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 generally similar to those seen in adult patients⁹. 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.

The safety and effectiveness of BRIVIACT in the treatment of partial-onset seizures have been established in patients four years of age and older. Use of BRIVIACT in these age groups is supported by evidence from placebo-controlled partial-onset seizure studies of BRIVIACT in adults with additional pharmacokinetic and open-label safety studies in pediatric patients age 4 to younger than 16 years of age. Partial-onset seizures in pediatric patients aged 4 to 16 years of age are similar to those in adults and a similar AED exposure-response relationship has been demonstrated. Weight-based dose adaptations have been established in the pediatric population to achieve similar plasma concentrations as observed in adults. The safety and tolerability profile for BRIVIACT in pediatric patients 4 to 16 years of age is generally similar to that seen with adult patients.⁹

The most common adverse reactions recorded for adults (at least 5 percent for BRIVIACT and at least 2 percent more frequently than placebo) are somnolence and sedation, dizziness, fatigue, and nausea and vomiting symptoms.⁹

For additional medical information about BRIVIACT, patient assistance, or any other information please visit www.BRIVIACT.com or call 1-844-599-2273.

About Epilepsy^{10,11,12,5}

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 U.S. more than 3.4 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. Around one third of patients with epilepsy currently 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 anti-epileptic 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 BRIVIACT^{9,13}

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 U.S., BRIVIACT® (brivaracetam) CV is indicated for the treatment of partial-onset seizures in patients 4 years of age and older. As the safety of BRIVIACT injection in pediatric patients has not been established, BRIVIACT injection is indicated for the treatment of partial-onset seizures only in adult patients (16 years of age and older).

In the European Union, BRIVIACT is approved as adjunctive therapy in the treatment of partial-onset seizures in patients 16 years of age and older with epilepsy. The European Medicines Agency has different regulatory requirements from FDA for approval of monotherapy indications.

Important Safety Information about BRIVIACT® in the U.S. ⁹

Warnings and Precautions

- **Suicidal Behavior and Ideation:** Anti-epileptic drugs, including BRIVIACT, increase the risk of suicidal behavior and ideation. Monitor patients taking BRIVIACT for the emergence or worsening of depression; unusual changes in mood or behavior; or suicidal thoughts, behavior, or self-harm. Advise patients, their caregivers, and/or families to be alert for these behavioral changes and report them immediately to a healthcare provider.
- **Neurological Adverse Reactions:** BRIVIACT causes somnolence, fatigue, dizziness, and disturbance in coordination. Somnolence and fatigue-related adverse reactions were reported in 25% of adult patients taking at least 50 mg per day of BRIVIACT compared to 14% of adult patients taking placebo. Dizziness and disturbance in gait and coordination were reported in 16% of adult patients taking at least 50 mg per day of BRIVIACT compared to 10% of adult patients taking placebo. The risk is greatest early in treatment but can occur at any time. Monitor patients for these signs and symptoms and advise them not to drive or operate machinery until they have gained sufficient experience on BRIVIACT.
- **Psychiatric Adverse Reactions:** BRIVIACT causes psychiatric adverse reactions, including non-psychotic and psychotic symptoms. These events were reported in approximately 13% of adult patients taking at least 50 mg per day of BRIVIACT compared to 8% of adult patients taking placebo. A total of 1.7% of adult patients taking BRIVIACT discontinued treatment due to psychiatric reactions compared to 1.3% of patients taking placebo. Psychiatric adverse reactions were also observed in open-label pediatric trials and were generally similar to those observed in adults. Advise patients to report these symptoms immediately to a healthcare provider.
- **Hypersensitivity:** BRIVIACT can cause hypersensitivity reactions. Bronchospasm and angioedema have been reported. Discontinue BRIVIACT if a patient develops a hypersensitivity reaction after treatment. BRIVIACT is contraindicated in patients with a prior hypersensitivity reaction to brivaracetam or any of the inactive ingredients.
- **Withdrawal of Anti-epileptic Drugs:** As with all anti-epileptic drugs, BRIVIACT should generally be withdrawn gradually because of the risk of increased seizure frequency and status epilepticus.

DOSING CONSIDERATIONS

- Dose adjustments are recommended for patients with all stages of hepatic impairment.
- When BRIVIACT is co-administered with rifampin, an increase in the BRIVIACT dose is recommended.

ADVERSE REACTIONS

In adult adjunctive therapy placebo-controlled clinical trials, the most common adverse reactions (at least 5% for BRIVIACT and at least 2% more frequently than placebo) were somnolence and sedation, dizziness, fatigue, and nausea and vomiting symptoms. Adverse reactions reported in clinical studies of pediatric patients 4 years to less than 16 years of age were generally similar to those in adult patients.

BRIVIACT is a Schedule V controlled substance.

Please refer to full Prescribing Information at <http://www.briviact.com/briviact-PI.pdf>.

For more information on BRIVIACT®, contact 844-599-CARE (2273).

BRIVIACT® is a registered trademark of the UCB Group of Companies.

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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 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 - UCB

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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