UCB News

UCB presents new data across expansive epilepsies portfolio at 15th European Epilepsy Congress (EEC)

- 16 scientific abstracts demonstrate UCB's ongoing commitment to advancing treatment and improving outcomes and experiences for people living with epilepsies
- Data provide insights on the use of FINTEPLA® (fenfluramine)▼[1] in Dravet syndrome and Lennox-Gastaut syndrome, brivaracetam[2] in focal-onset seizures, and *Staccato® alprazolam[3] (an investigational treatment for potential termination of prolonged epileptic seizures)
- There is additional focus on unmet needs in LGS in Europe, including the need for an earlier diagnosis
- Further research looks at the mental health of caregivers supporting people living with Dravet syndrome, and expert consensus recommendations on seizure emergencies suitable for Rapid and Early Seizure Termination

Brussels, Belgium – 6 September 2024 – 7:00 AM CET– UCB today announced it will showcase 16 abstracts highlighting its broad research program at the 15th European Epilepsy Congress (EEC), September 7-11, 2024 (Rome, Italy). The comprehensive and diverse data set includes clinical and real-world data, medical and patient research, and key areas of current unmet need.

Dr Konrad Werhahn, Global Medical Affairs, UCB, commented: "It's a privilege to be able to showcase UCB's latest research at the European Epilepsy Congress. The data reflect the breadth of our epilepsies portfolio and our commitment to advancing knowledge so we can better treat a diverse range of patients. We recognize that more still needs to be done to improve the care of people living with epilepsy and rare epilepsy syndromes, and we will continue to champion innovative industry-leading research to make a difference in the lives of patients and their families."

Data to be presented at the 15th European Epilepsy Congress (EEC)

Dravet syndrome

Fenfluramine data focused on Dravet syndrome (DS) include a model of the effectiveness of the treatment[4], an analysis of safety, tolerability and clinical global impression-improvement scale ratings in adult patients[5], an evaluation of healthcare utilization in US patients treated with the therapy,[6] and an assessment of factors affecting systemic exposure to the treatment, including patient characteristics and additional anti-seizure medications, to help healthcare professionals select an appropriate dose.[7] Furthermore, a literature review examines the mental health of caregivers supporting people living with DS.[8]

Lennox-Gastaut syndrome

Fenfluramine data focused on Lennox-Gastaut syndrome (LGS) include a post hoc analysis of the benefits received from treatment in terms of seizure-free days,[9] and an evaluation of the pharmacokinetics of fenfluramine and norfenfluramine (active metabolite) dosages and exposures in pediatric and adult patients.[10] Additionally, a European real-world study provide further insight on patient profiles and unmet needs in LGS,[11] and the process for developing a new electronic decision-assisting tool**, with a group of ten epilepsy experts,

Date of preparation: July 2024
GL-BR-2400003

which aims to help physicians evaluate the likelihood that their patient has Lennox-Gastaut syndrome and suggest them to initiate further validation steps.[12]

Focal-onset seizures
Data presented on brivaracetam include explorations of long-term treatment outcomes in pediatric populations with focal-onset seizures and cognitive or learning comorbidities in an open-label extension study,[13] and in adult populations with focal epilepsy of different etiologies.[14] Furthermore, data from a 12-month prospective non-interventional study evaluating brivaracetam clinical outcomes,[15] and patient quality of life when used in early treatment lines will also be presented.[16]

Rapid and early seizure termination
Expert consensus recommendations will be shared on Rapid and Early Seizure Termination (REST), a potential new treatment approach to prevent progression of epileptic seizures to seizure emergencies. The recommendations also address the types of seizures that warrant REST medication as well as the optimal timing for intervention.[17]

Pipeline programs
Data on the investigational therapy *Staccato® alprazolam include an evaluation of the pharmacokinetics and tolerability of the treatment to support dose selection for adolescents with epilepsy,[18] and an assessment of the pulmonary safety of the treatment in healthy participants and those with mild asthma.[19]

Symposium
The 15th EEC will feature one UCB-supported symposium:

- It's Time to Talk: Monday, 9th September 13:45-15:00 CET. Focusing on Developmental and Epileptic Encephalopathies (DEEs), including the latest treatment guidelines in LGS, building awareness of the condition, a new digital screening tool and the importance of early and adult diagnosis.

UCB presentations during the 15th EEC

Lead Author	Abstract Title
Fenfluramine	
Mittur A, et al.	Modeling systemic exposure to fenfluramine and its active metabolite, norfenfluramine, in patients with Dravet syndrome
Mittur A, et al.	Pharmacokinetics of fenfluramine and its active metabolite norfenfluramine in patients with Lennox-Gastaut syndrome
Auvin S, et al.	Fenfluramine increases seizure-free days in patients with Lennox-Gastaut syndrome
Scheffer IE, et al.	Analysis of safety, tolerability and clinical global impression-improvement scale ratings in patients with Dravet syndrome enrolled as adults in a fenfluramine open-label extension study
Arteaga Duarte C, et al.	Comparative effectiveness of fenfluramine versus cannabidiol: Analysis on numbers needed to treat
Ems D, et al.	Healthcare utilization and persistence in patients with Dravet syndrome: A retrospective analysis using US claims data
Brivaracetam	
Knake S, et al.	Brivaracetam adjunctive therapy in earlier treatment lines in adults with focal-onset seizures in Europe and Canada: second interim results of 12-month real-world data from BRITOBA

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GL-BR-2400003

Winter Y, et al.	Treatment satisfaction, work productivity, and quality of life under adjunctive brivaracetam in earlier treatment lines in adults with focal-onset seizures: 12-month real-world data from BRITOBA
Lagae L, et al.	Long-term efficacy and tolerability of brivaracetam in pediatric patients with focal-onset seizures and cognitive or learning comorbidities: Post hoc analysis of an open-label trial
Dave H, et al.	Effectiveness and tolerability of brivaracetam in adults with epilepsy etiology of cerebral neoplasm, cerebrovascular accident or cranial trauma: Pooled data analyses from two real-world studies
Disease burden and patient need	
Strzelczyk A, et al.	Insights into Lennox-Gastaut syndrome: A European real-world study on patient profiles and unmet needs
Jacob B, et al.	Evaluating mental health in caregivers of patients with Dravet syndrome: A systematic review
Pina Garza JE, et al.	Expert consensus recommendations on seizure emergencies suitable for rapid and early seizure termination (rest) and timing of intervention
Arzimanoglou A, et al.	Development of an Electronic Diagnostic Criteria Tool for Lennox-Gastaut Syndrome (LGS)
Staccato® alprazolam	
Miller D, et al.	Pulmonary safety of *Staccato® alprazolam in healthy participants and participants with mild asthma: Phase 1, randomized, double-blind, placebo-controlled trial
Klein P, et al.	Pharmacokinetics and tolerability of single-dose *Staccato® alprazolam in adolescents with epilepsy and population pk analysis to support dose selection in adolescents

*The safety and efficacy of Staccato® alprazolam have not been established and it is not currently approved for use in this indication by any regulatory authority worldwide.

**For healthcare professionals only. The LGS questionnaire has been developed by a group of epilepsy experts. Its digitalization has been funded by UCB, with no influence on its content and validated by the same epilepsy experts.

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Driven by science.

Date of preparation: July 2024
GL-BR-2400003

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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 approximately 9,000 people in approximately 40 countries, the company generated revenue of €5.3 billion in 2023. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news.

Important Safety Information about FINTEPLA▼ (fenfluramine) in the EU[1]

Indications: Treatment of seizures associated with Dravet syndrome and Lennox-Gastaut syndrome as an add-on therapy to other anti-epileptic medicines for patients 2 years of age and older.

Dosage and Administration: Please refer to SmPC for full information. Should be initiated and supervised by physicians with experience in the treatment of epilepsy. Fintepla is prescribed and dispensed according to the Fintepla controlled access programme. Dravet syndrome: Patients who are **not** taking stiripentol: Starting dose is 0.1 mg/kg twice daily (0.2 mg/kg/day). After 7 days, if tolerated, can increase dose to 0.2 mg/kg twice daily (0.4 mg/kg/day). After an additional 7 days, if tolerated and further seizure reduction required, can increase dose to a maximum of 0.35 mg/kg twice daily (0.7 mg/kg/day), which is the recommended maintenance dose. Patients requiring more rapid titration may increase the dose every 4 days. Do not exceed maximum daily dose of 26 mg (13 mg twice daily). Patients who are taking stiripentol: Starting dose is 0.1 mg/kg twice daily (0.2 mg/kg/day). After 7 days, if tolerated, can increase dose to 0.2 mg/kg twice daily (0.4 mg/kg/day), which is the recommended maintenance dose. Patients requiring more rapid titration may increase the dose every 4 days. Do not exceed a total dose of 17 mg (8.6 mg twice daily). Lennox-Gastaut syndrome: Starting dose is 0.1 mg/kg twice daily (0.2 mg/kg/day). After 7 days, the dose should be increased to 0.2 mg/kg twice daily (0.4 mg/kg/day), if tolerated. After an additional 7 days, if tolerated, dose should be increased to 0.35 mg/kg twice daily (0.7 mg/kg/day), which is the recommended maintenance dose. Do not exceed maximum daily dose of 26 mg (13 mg twice daily). Discontinuation: When discontinuing treatment, decrease the dose gradually. As with all anti-epileptic medicines, avoid abrupt discontinuation when possible to minimize the risk of increased seizure frequency and status epilepticus. A final echocardiogram should be conducted 3-6 months after the last dose of treatment with fenfluramine. Renal impairment: Generally, no dose adjustment is recommended when administered to patients with mild to severe renal impairment, however, a slower titration may be considered. If adverse reactions are reported, a dose reduction may be needed. Has not been studied in patients with end-stage renal disease. Not known if fenfluramine or its active metabolite, norfenfluramine, is dialyzable. Hepatic impairment: Hepatic impairment: Generally, no dose adjustment is recommended when Fintepla is administered without concomitant stiripentol to patients with mild and moderate hepatic impairment (Child-Pugh Class A and B). In patients with severe hepatic impairment (Child-Pugh C) not receiving concomitant stiripentol, the maximum dosage is 0.2mg/kg twice daily, and the maximal total daily dose is 17 mg. There are limited clinical data on the use of Fintepla with stiripentol in patients with mild impaired hepatic function. A slower titration may be considered in patients with hepatic impairment and a dose reduction may be needed if adverse reactions are reported. No clinical data is available on the use of Fintepla with stiripentol in moderate and severe hepatic impairment, therefore not recommended for use. Elderly: No data available. Paediatric population: Safety and efficacy in children below 2 years of age not yet established. No data available. **Contraindications:** Hypersensitivity to active substance or any excipients. Aortic or mitral valvular heart disease and pulmonary arterial hypertension. Within 14 days of the administration of monoamine oxidase inhibitors due to an increased risk of serotonin

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syndrome. **Warnings and Precautions:** Aortic or mitral valvular heart disease and pulmonary arterial hypertension: Prior to starting treatment, patients must undergo an echocardiogram to establish a baseline and exclude any pre-existing valvular heart disease or pulmonary hypertension. Conduct echocardiogram monitoring every 6 months for the first 2 years and annually thereafter. If an echocardiogram indicates pathological valvular changes, consider follow-up earlier to evaluate whether the abnormality is persistent. If pathological abnormalities seen on echocardiogram, evaluate the benefit versus risk of continuing fenfluramine treatment with the prescriber, caregiver and cardiologist. Once treatment is discontinued for any reasons, a final echocardiogram should be conducted 3-6 months after the last dose of treatment with fenfluramine. If echocardiogram findings suggestive of pulmonary arterial hypertension, perform a repeat echocardiogram as soon as possible and within 3 months to confirm these findings. If echocardiogram finding is confirmed suggestive of an increased probability of pulmonary arterial hypertension defined as intermediate probability, conduct a benefit-risk evaluation of continuation of Fintepla by the prescriber, carer and cardiologist. If echocardiogram suggests a high probability, it is recommended fenfluramine treatment should be stopped. Decreased appetite and weight loss: Fenfluramine can cause decreased appetite and weight loss - an additive effect can occur in combination with other anti-epileptic medicines such as stiripentol. Monitor the patient's weight. Undertake risk-benefit evaluation before starting treatment if history of anorexia nervosa or bulimia nervosa. Fintepla controlled access programme: A controlled access programme has been created to 1) prevent off-label use in weight management in obese patients and 2) confirm that prescribing physicians have been informed of the need for periodic cardiac monitoring in patients taking Fintepla. Somnolence: Fenfluramine can cause somnolence which could be potentiated by other central nervous system depressants. Suicidal behaviour and ideation: Suicidal behaviour and ideation have been reported in patients treated with anti-epileptic medicines in several indications. Advise patients and caregivers to seek medical advice should any signs of suicidal behaviour and ideation emerge. Serotonin syndrome: Serotonin syndrome, a potentially life-threatening condition, may occur with fenfluramine treatment, particularly with concomitant use of other serotonergic agents; with agents that impair metabolism of serotonin such as MAOIs; or with antipsychotics that may affect the serotonergic neurotransmitter systems. Carefully observe the patient, particularly during treatment initiation and dose increases. Increased seizure frequency: A clinically relevant increase in seizure frequency may occur during treatment, which may require adjustment in the dose of fenfluramine and/or concomitant anti-epileptic medicines, or discontinuation of fenfluramine, should the benefit-risk be negative. Cyproheptadine: Cyproheptadine is a potent serotonin receptor antagonist and may therefore decrease the efficacy of fenfluramine. If cyproheptadine is added to treatment with fenfluramine, monitor patient for worsening of seizures. If fenfluramine treatment is initiated in a patient taking cyproheptadine, fenfluramine's efficacy may be reduced. Glaucoma: Fenfluramine can cause mydriasis and can precipitate angle closure glaucoma. Discontinue therapy in patients with acute decreases in visual acuity. Consider discontinuation if ocular pain of unknown origin. Effect of CYP1A2 or CYP2B6 inducers: Co-administration with strong CYP1A2 inducers or CYP2B6 inducers will decrease fenfluramine plasma concentrations, which may lower the efficacy of fenfluramine. If co-administration is considered necessary, the patient should be monitored for reduced efficacy and a dose increase of fenfluramine could be considered provided that it does not exceed twice the maximum daily dose (52 mg/day). If a strong CYP1A2 or CYP2B6 inducer is discontinued during maintenance treatment with fenfluramine, consider gradual reduction of the fenfluramine dosage to the dose administered prior to initiating the inducer. Effect of CYP1A2 or CYP2D6 inhibitors: Initiation of concomitant treatment with a strong CYP1A2 or CYP2D6 inhibitor may result in higher exposure and, therefore, adverse events should be monitored, and a dose reduction may be needed in some patients. Excipients: Contains sodium ethyl para-hydroxybenzoate (E 215) and sodium methyl para-hydroxybenzoate (E 219) - may cause allergic reactions (possibly delayed). It also contains sulfur dioxide (E 220) which may rarely cause severe hypersensitivity reactions and bronchospasm. Patients with rare glucose-galactose malabsorption should not take this medicine. The product contains less than 1 mmol sodium (23 mg) per the maximum daily dose of 12 mL;

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essentially 'sodium-free'. Contains glucose - may be harmful to teeth. Interactions: Pharmacodynamic interactions with other CNS depressants increase the risk of aggravated central nervous system depression. An increase in dose may be necessary when coadministered with rifampicin or a strong CYP1A2 or CYP2B6 inducer. In in vitro studies coadministration with a strong CYP1A2 or CYP2D6 inhibitor may result in higher exposure (see section 4.4 of the SmPC). Coadministration with CYP2D6 substrates or MATE1 substrates may increase their plasma concentrations. Co-administration with CYP2B6 or CYP3A4 substrates may decrease their plasma concentrations. Pregnancy and lactation: Limited data in pregnant women. As a precaution, avoid use of Fintepla in pregnancy. It is unknown whether fenfluramine/metabolites are excreted in human milk. Animal data have shown excretion of fenfluramine/metabolites in milk. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Fintepla taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. Drive and use machines.: Fintepla has moderate influence on the ability to drive/ use machines as it may cause somnolence and fatigue. Advise patients not to drive or operate machinery until they have sufficient experience to gauge whether it adversely affects their abilities. **Adverse effects:** Dravet syndrome: Very common (≥1/10): Upper respiratory tract infection, decreased appetite, somnolence, diarrhoea, pyrexia, fatigue, blood glucose decreased, echocardiogram abnormal (Consisted of trace and mild mitral regurgitation, and trace aortic regurgitation, which are considered physiologic). Common (≥1/100 to <1/10): Bronchitis, abnormal behaviour, aggression, agitation, insomnia, mood swings, ataxia, hypotonia, lethargy, seizure, status epilepticus, tremor, constipation, salivary hypersecretion, weight decreased and blood prolactin increased. Lennox-Gastaut syndrome: Very common (≥1/10): Upper respiratory tract infection, decreased appetite, somnolence, diarrhoea, vomiting, fatigue. Common (≥1/100 to <1/10): Bronchitis, influenza, pneumonia, seizure, status epilepticus, lethargy, tremor, constipation, salivary hypersecretion, blood prolactin increased, weight decreased, fall. Refer to SmPC for other adverse reactions.

▼*This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.*

Refer to the European Summary of Product Characteristics for other adverse reactions and full Prescribing Information.
https://www.ema.europa.eu/en/documents/product-information/fintepla-epar-product-information_en.pdf

Important Safety Information about BRIVIACT® (brivaracetam) in the EU[2]

Therapeutic indications: BRIVIACT is indicated as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 2 years of age with epilepsy.

Posology and method of administration: The physician should prescribe the most appropriate formulation and strength according to weight and dose. It is recommended to parent and care giver to administer BRIVIACT oral solution with the measuring device (10 ml or 5 ml oral dosing syringe) provided in the carton box. BRIVIACT solution for injection/infusion is an alternative route of administration for patients when oral administration is temporarily not feasible. There is no experience with twice daily intravenous administration of brivaracetam for a period longer than 4 days. Adults: The recommended starting dose is 50 or 100 mg/day based on physician's assessment of required for seizure reduction versus potential side effects. Brivaracetam can be taken with or without food. Based on individual patient response and tolerability, the dose may be adjusted in the effective dose range of 50 mg/day to 200 mg/day. Children and adolescents weighing 50 kg or more: The recommended starting dose is 50 mg/day. Brivaracetam may also be initiated at 100 mg/day based

Date of preparation: July 2024
GL-BR-2400003

on physician's assessment of need for seizure control. The recommended maintenance dose is 100 mg/day. Based on individual patient response, the dose may be adjusted in the effective dose range of 50 mg/day to 200 mg/day. Children and adolescents weighing from 20 kg to less than 50 kg: The recommended starting dose is 1 mg/kg/day. Brivaracetam may also be initiated at doses up to 2 mg/kg/day based on physician's assessment of need for seizure control. The recommended maintenance dose is 2 mg/kg/day. Based on individual patient response, the dose may be adjusted in the effective dose range of 1 mg/kg/day to 4 mg/kg/day. Children weighing from 10 kg to less than 20 kg: The recommended starting dose is 1 mg/kg/day. Brivaracetam may also be initiated at doses up to 2.5 mg/kg/day based on physician's assessment of need for seizure control. The recommended maintenance dose is 2.5 mg/kg/day. Based on individual patient response, the dose may be adjusted in the effective dose range of 1 mg/kg/day to 5 mg/kg/day. For adults, adolescents and children from 2 years of age, the dose should be administered in two equally divided doses, approximately 12 hours apart.

If patients miss one dose or more, it is recommended that they take a single dose as soon as they remember and take the following dose at the usual morning or evening time. Brivaracetam oral solution can be diluted in water or juice shortly before swallowing; a nasogastric tube or a gastrostomy tube may also be used. Brivaracetam may be initiated with either intravenous or oral administration. When converting from oral to intravenous administration or vice versa, the total daily dose and frequency of administration should be maintained. Brivaracetam may be administered as an intravenous bolus without dilution or diluted in a compatible diluent and administered as a 15-minute intravenous infusion. This medicinal product must not be mixed with other medicinal products. Brivaracetam bolus injection or intravenous infusion has not been studied in acute conditions, e.g. status epilepticus, and is therefore not recommended for such conditions. For patients from 16 years of age, if brivaracetam has to be discontinued, it is recommended that the dose is reduced gradually by 50 mg/day on a weekly basis. For patients below the age of 16 years, if brivaracetam has to be discontinued, it is recommended that the dose is reduced by a maximum of half the dose every week until a dose of 1 mg/kg/day (for patients with a body weight less than 50 kg) or 50 mg/day (for patients with body weight of 50 kg or more) is reached. After 1 week of treatment at 50 mg/day, a final week of treatment at 20 mg/day is recommended. No dose adjustment is needed for elderly patients (≥65 years of age) or for those with renal impairment. Based on data in adults, no dose adjustment is necessary in paediatric patients with impaired renal function. No clinical data are available on paediatric patients with renal impairment. Brivaracetam is not recommended for patients with end-stage renal disease undergoing dialysis due to lack of data. Exposure to brivaracetam was increased in patients with chronic liver disease. In patients with hepatic impairment, the following adjusted doses, administered in 2 divided doses, approximately 12 hours apart, are recommended for all stages of hepatic impairment: In adults, adolescents and children weighing ≥50 kg, a 50 mg/day starting dose is recommended, with a maximum daily dose of 150 mg/day. For adolescents and children weighing from 20 kg to <50 kg, a 1 mg/kg/day is recommended, with a maximum daily dose of 3 mg/kg/day. For children weighing from 10 kg to <20 kg, a 1 mg/kg/day is recommended, with a maximum daily dose of 4 mg/kg/day. No clinical data are available in paediatric patients with hepatic impairment. The efficacy of brivaracetam in paediatric patients aged less than 2 years has not yet been established.

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 brivaracetam. Patients should be monitored for signs of suicidal ideation and behaviours 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. Clinical data on the use of brivaracetam in patients with pre-existing hepatic

Date of preparation: July 2024
GL-BR-2400003

impairment are limited. Dose adjustments are recommended for patients with hepatic impairment. Brivaracetam film-coated tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take brivaracetam. Brivaracetam film-coated tablets, solution for injection/infusion and oral solution contain less than 1 mmol sodium (23mg) per tablet/vial/ml respectively, that is to say essentially 'sodium free'. Brivaracetam oral solution contains 168 mg sorbitol (E420) in each ml. Patients with hereditary fructose intolerance (HFI) should not take this medicinal product. The oral solution contains methyl parahydroxybenzoate (E218), which may cause allergic reactions (possibly delayed). Brivaracetam oral solution contains propylene glycol (E1520).
Interaction with other medicinal products and other forms of interaction: In clinical studies, although patient numbers were limited, brivaracetam had no observed benefit over placebo among patients taking concomitant levetiracetam. No additional safety or tolerability concern was observed. In an interaction study between brivaracetam 200 mg single dose and ethanol 0.6 g/L continuous infusion in healthy volunteers, there was no pharmacokinetic interaction, but the effect of alcohol on psychomotor function, attention and memory was approximately doubled with the intake of brivaracetam. Intake of brivaracetam with alcohol is not recommended. In vitro data suggest that brivaracetam has a low interaction potential. The main disposition pathway of brivaracetam® is by CYPindependent hydrolysis; a second pathway involves hydroxylation mediated by CYP2C19. Brivaracetam plasma concentrations may increase when co-administered with CYP2C19 strong inhibitors (e.g. fluconazole, fluvoxamine), but the risk of a clinically relevant CYP2C19 mediated interaction is considered to be low. Limited clinical data are available implying that coadministration of cannabidiol may increase the plasma exposure of brivaracetam, possibly through CYP2C19 inhibition, but the clinical relevance is uncertain. In healthy subjects, co-administration with the strong enzyme inducer rifampicin (600 mg/day for 5 days), decreased brivaracetam area under the plasma concentration curve (AUC) by 45%. Prescribers should consider adjusting the dose of brivaracetam in patients starting or ending treatment with rifampicin. Brivaracetam plasma concentrations are decreased when co-administered with strong enzyme-inducing AEDs (carbamazepine, phenobarbital, phenytoin) but no dose adjustment is required. Other strong enzyme inducers such as St John's wort (Hypericum perforatum) may decrease the systemic exposure of brivaracetam. Starting or ending treatment with St John's wort should be done with caution. Brivaracetam at 50 or 150 mg/day did not affect the AUC of midazolam (metabolised by CYP3A4). The risk of clinically relevant CYP3A4 interactions is considered low. In vitro studies have shown that brivaracetam exhibits little or no inhibition of CYP450 isoforms except for CYP2C19 and may therefore increase plasma concentrations of medicinal products metabolised by CYP2C19 (e.g. lansoprazole, omeprazole, diazepam). Brivaracetam did not induce CYP1A1/2 but induced CYP3A4 and CYP2B6 in vitro. No CYP3A4 induction was found in vivo. CYP2B6 induction has not been investigated in vivo and brivaracetam may decrease plasma concentrations of medicinal products metabolised by CYP2B6 (e.g. efavirenz). In vitro interaction studies to determine the potential inhibitory effects on transporters concluded that there were no clinically relevant effects, except for OAT3. In vitro, brivaracetam inhibits OAT3 with a half maximal inhibitory concentration 42-fold higher than the Cmax at the highest clinical dose. Brivaracetam 200 mg/day may increase plasma concentrations of medicinal products transported by OAT3. Brivaracetam is a moderate reversible inhibitor of epoxide hydrolase, resulting in an increased concentration of carbamazepine epoxide, an active metabolite of carbamazepine. In controlled clinical studies, carbamazepine epoxide plasma concentration increased by a mean of 37%, 62% and 98% with little variability at Brivaracetam doses of 50 mg/day, 100 mg/day and 200 mg/day, respectively. No safety risks were observed. There was no additive effect of brivaracetam and valproate on the AUC of carbamazepine epoxide. No dose adjustment is needed when brivaracetam is co-administered with carbamazepine, phenobarbital or phenytoin. Brivaracetam had no clinically relevant effect on the plasma concentrations of clobazam, clonazepam, lacosamide, lamotrigine, levetiracetam, oxcarbazepine, phenobarbital, phenytoin, pregabalin, topiramate, valproic acid or zonisamide. There are no data available on the effects of clobazam, clonazepam, lacosamide, pregabalin or zonisamide on brivaracetam

plasma concentrations. Co-administration of brivaracetam (100 mg/day) with an oral contraceptive containing ethinylestradiol (0.03 mg) and levonorgestrel (0.15 mg) did not influence the pharmacokinetics of either substance. However, when brivaracetam was coadministered at a dose of 400 mg/day (twice the recommended maximum daily dose), a reduction in estrogen and progestin AUCs of 27% and 23%, respectively, was observed without impact on suppression of ovulation. **Pregnancy:** Data on the use of brivaracetam in pregnant women are limited. There are no data on placental transfer in humans, but brivaracetam was shown to readily cross the placenta in rats. The potential risk for humans is unknown. Animal studies did not detect any teratogenic potential of brivaracetam. In clinical studies, adjunctive brivaracetam used concomitantly with carbamazepine induced a dose-related increase in the concentration of the active metabolite, carbamazepine-epoxide. There are insufficient data to determine the clinical significance of this effect in pregnancy. Brivaracetam should not be used during pregnancy unless clinically necessary. **Breast-feeding:** Brivaracetam is excreted in human breast milk. The decision to discontinue either breastfeeding or brivaracetam should be made based on the benefit of the medicinal product to the mother. In case of co-administration of brivaracetam and carbamazepine, the amount of carbamazepine-epoxide excreted in breast milk could increase. The clinical significance remains unknown. **Fertility:** No human data on the effect of brivaracetam on fertility are available. There was no effect on fertility in rats. **Effects on ability to drive and use machines**: Brivaracetam 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 brivaracetam on their ability to perform such activities. **Undesirable effects:** The most frequently reported adverse reactions with brivaracetam were somnolence (14.3%) and dizziness (11.0%); they were usually mild-to-moderate in intensity. Somnolence and fatigue were reported at a higher incidence with increasing dose. Very common adverse reactions (≥1%-<10%) were influenza, decreased appetite, depression, anxiety, insomnia, irritability, convulsion, vertigo, upper respiratory tract infections, cough, nausea, vomiting, constipation and fatigue. Neutropenia was reported in 6/1099 (0.5%) of brivaracetam and none (0/459) of the placebo-treated patients. Four of these subjects had decreased neutrophil counts at baseline. None of the neutropenia cases were severe, required any specific treatment or led to discontinuation of brivaracetam and none had associated infections. Suicidal ideation was reported in 0.3% (3/1099) of brivaracetam and 0.7% (3/459) of placebo-treated patients. In short-term clinical studies of brivaracetam in patients with epilepsy, there were no cases of completed suicide and suicide attempt; however, both were reported in open-label extension studies. The safety profile of brivaracetam observed in children from 1 month of age was consistent with the safety profile observed in adults. In the open label, uncontrolled, long-term studies suicidal ideation was reported in 4.7 % of paediatric patients (assessed from 6 years onwards, more common in adolescents) compared with 2.4 % of adults and behavioural disorders were reported in 24.8 % of paediatric patients compared with 15.1 % of adults. The majority of events were mild or moderate in intensity, were non-serious, and did not lead to discontinuation of study drug. An additional adverse reaction reported in children was psychomotor hyperactivity (4.7 %). No specific pattern of adverse event (AE) was identified in children from 1 month to < 4 years of age when compared to older paediatric age groups. No significant safety information was identified indicating the increasing incidence of a particular AE in this age group. As data available in children younger than 2 years of age are limited, brivaracetam is not indicated in this age range. Limited clinical data are available in neonates. Reactions suggestive of immediate (Type I) hypersensitivity have been reported in a small number of brivaracetam patients (9/3022) during clinical development. **Overdose:** There is limited clinical experience with brivaracetam overdose in humans. Somnolence and dizziness have been reported in a healthy subject taking a single dose of 1,400 mg of brivaracetam. The following adverse reactions were reported with brivaracetam overdose: nausea, vertigo, balance disorder, anxiety, fatigue, irritability, aggression, insomnia, depression, and suicidal ideation in the postmarketing experience. In general, the adverse reactions associated with brivaracetam overdose were consistent with the known adverse reactions. There is no specific

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antidote for overdose with brivaracetam. Treatment of an overdose should include general supportive measures. Since <10% of brivaracetam is excreted in urine, haemodialysis is not expected to significantly enhance brivaracetam clearance.

Refer to the European Summary of Product Characteristics for other adverse reactions and full Prescribing Information.
https://www.ema.europa.eu/en/documents/product-information/briviact-epar-product-information_en.pdf

Forward looking statements
This press release may contain forward-looking statements including, without limitation, statements containing the words "believes", "anticipates", "expects", "intends", "plans", "seeks", "estimates", "may", "will", "continue" and similar expressions. These forward-looking statements are based on current plans, estimates and beliefs of management. All statements, other than statements of historical facts, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial information, expected legal, arbitration, political, regulatory or clinical results or practices and other such estimates and results. By their nature, such forward-looking statements are not guarantees of future performance and are subject to known and unknown risks, uncertainties and assumptions which might cause the actual results, financial condition, performance or achievements of UCB, or industry results, to differ materially from those that may be expressed or implied by such forward-looking statements contained in this press release. Important factors that could result in such differences include: the global spread and impact of COVID-19, changes in general economic, business and competitive conditions, the inability to obtain necessary regulatory approvals or to obtain them on acceptable terms or within expected timing, 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, safety, quality, data integrity or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, product liability claims, challenges to patent protection for products or product candidates, competition from other products including biosimilars, 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. There is no guarantee that new product candidates will be discovered or identified in the pipeline, will progress to product approval or that new indications for existing products will be developed and approved. Movement from concept to commercial product is uncertain; preclinical results do not guarantee safety and efficacy of product candidates in humans. So far, the complexity of the human body cannot be reproduced in computer models, cell culture systems or animal models. The length of the timing to complete clinical trials and to get regulatory approval for product marketing has varied in the past and UCB expects similar unpredictability going forward. Products or potential products, which are the subject of partnerships, joint ventures or licensing collaborations may be subject to differences disputes between the partners or may prove to be not as safe, effective or commercially successful as UCB may have believed at the start of such partnership. UCB's efforts to acquire other products or companies and to integrate the operations of such acquired companies may not be as successful as UCB may have believed at the moment of acquisition. Also, UCB or others could discover safety, side effects or manufacturing problems with its products and/or devices after they are marketed. The discovery of significant problems with a product similar to one of UCB's products that implicate an entire class of products may have a material adverse effect on sales of the entire class of affected products. Moreover, sales may be impacted by international and domestic trends toward managed care and health care cost containment, including pricing

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