UCB News

UCB presents new data advancing patient-focused scientific leadership at American Epilepsy Society Annual Meeting

- UCB will present 29 abstracts, including 4 late breakers, at American Epilepsy Society Annual Meeting 2023 highlighting clinical, health economic and demographic studies in epilepsy
- Presentations showcase diversity, potential and momentum of UCB's epilepsy and rare syndromes portfolio, including important fenfluramine and brivaracetam data
- Broad data sets reveal insights into different epilepsy types and different populations living with epilepsies
- Molecular, clinical, and real-world research focuses on current and future patient needs in epilepsy

Brussels, Belgium, 1 December 2023 – 7.00 AM (CET) – UCB (Euronext Brussels: UCB), a global biopharmaceutical company, today unveiled its extensive program of 29 studies, including 4 late breakers, accepted for presentation at the AES Annual Meeting 2023, taking place from 1-5 December in Orlando, Florida, USA.

"The data being presented at this year's American Epilepsy Society meeting highlight UCB's commitment to transforming outcomes and experiences for people living with epilepsies, redefining the future of epilepsy care. We are proud of the innovation and impact we have been able to deliver over the past three decades with our evolving portfolio of innovative medicines, and look forward to continuing to partner with patients, carers, and the scientific community to address unmet needs and advance the next generation of epilepsy care," said Mike Davis, Global Head of Epilepsy & Rare Syndromes, UCB.

Key scientific and patient-focused data include:

- In focal-onset seizures (FOS) - interim data from a post-marketing non-interventional study on effectiveness and quality of life (QoL) with adjunctive brivaracetam in earlier treatment lines.
- In Dravet syndrome - an analysis from an open-label extension study of adults treated with fenfluramine.
- In Lennox-Gastaut syndrome - a post hoc analysis evaluating the percentage of seizure-free days in patients treated with fenfluramine in the 14-week randomized control trial and its open-label extension (median treatment direction, 1 year).
- In prolonged seizures - three studies evaluating the safety, tolerability, and pharmacokinetics of single-use inhaled alprazolam (an investigational treatment for potential termination of prolonged epileptic seizures) in different populations.
- In SUDEP (Sudden Unexpected Death in Epilepsy) - a literature review highlighting the differences in provision of information between healthcare professionals and patients.
- In disease management - data from early research into mechanisms underlying Developmental and Epileptic Encephalopathies (DEE).
- In health equity - results from a survey of US neurologists on health disparities in black patients living with epilepsy.

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"Knowledge illuminates a path toward innovative solutions and transformative breakthroughs. At this year's American Epilepsy Society meeting, we converge not just as researchers and clinicians, but as pioneers of progress. For three decades, we've been committed to people living with epilepsy and their families. We aim for a future where every discovery moves us closer to a seizure-free life. In unity, we work to surround the patient and caregiver through every step of their care journey – from diagnosis to treatment to support in helping them navigate those moments in their lives that matter most," said Brad Chapman, Head of U.S. Epilepsy and Rare Syndromes.

Symposia and CME

UCB will be hosting a symposium on 2 December at 18:00 ET entitled "The 'window of opportunity': Recognizing the importance of rapid and early seizure termination", to shed further light on seizure emergencies and data being presented at AES on the *Seizure Termination Project*.* The project consists of an expert consensus group sharing best practice for rapid and early seizure termination (REST) to prevent progression to a higher-level emergency.

UCB is also supporting a CME program entitled 'Beyond Seizures: The Evolving Standard of Care in Developmental and Epileptic Encephalopathies' taking place on 1 December.

UCB data presentations at AES 2023

Saturday, December 2, 2023 (12:00 PM –2:00 PM ET)

Poster number and title		Authors
1.006	ΔFosB is part of a homeostatic mechanism that protects the epileptic brain from further deterioration	Clasadonte J, Mairet-Coello G, Stephens GS, Deprez T, Cortin PY, Boutier M, Frey A, Chin J, Rajman M
1.112	Electrophysiological and Behavioral Phenotypic Characterization of a Transgenic Mouse Model Associated with Syntaxin Binding protein-1 (STXBP1) Developmental and Epileptic Encephalopathy (DEE)	Rodriguez N, Van Den Herrewegen Y, Clasadonte J, Wolff C, Vallette B, Gomes AR, Mairet-Coello G, Widya M, Dedeurwaerdere S
1.286	Efficacy and Tolerability of Adjunctive Brivaracetam in Asian Patients With Focal Onset Seizures: A Phase 3 Randomized, Placebo-Controlled Trial	Inoue Y, Tiamkao S, Zhou D, Cabral-Lim L, Lim KS, Lim SH, Tsai JJ, Moseley B, Wang L, Sun W, Hayakawa Y, Sasamoto H, Sano T, McClung C, Bass A
1.290	Safety and Effectiveness of Lacosamide Monotherapy in Chinese Patients With Focal-Onset Seizures: Interim Results from a Real-World Study	Wu X, Wang D, Wang S, Schulz AL, Yu Y, Besson H, Chen S, Zhou D, Jiang Y
1.296	12-Month Effectiveness and Tolerability of Brivaracetam in Patients With Epilepsy and Cognitive or Psychiatric Comorbidities: Subgroup Data From the International EXPERIENCE Pooled Analysis	Villanueva V, D'Souza W, Faught E, Klein P, Reuber M, Rosenow F, Salas-Puig J, Soto-Insuga V, Strzelczyk A, Szaflarski JP, Besson H, Bourikas D, Daniels T, Floricel F, Friesen D, Laloyaux C, Sendersky V, Steinhoff BJ
1.303	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	Dave H, Sperling MR, Moseley B, Elmoufti S, Little A, Bourikas D, Steinhoff BJ
1.304	Expert Consensus Recommendations on Seizure Emergencies Suitable for Rapid and Early Seizure Termination (REST) and Timing of Intervention	Pina-Garza JE, Chez M, Cloyd J, Hirsch LJ, Kälviäinen R, Klein P, Lagae L, Sankar R, Specchio N, Strzelczyk A, Toledo M, Trinka E

Date of preparation: November 2023
GL-BR-2300007

1.374	A Survey of Rare Epilepsy Parents and Adult Siblings: To Assess Resources Needed to Prepare Families Living in the U.S. for Long-term Adult Care Planning for Their Loved One	Andrade DM, Bailey LD, Meskis MA, Hood V, Ferreira S, Dixon-Salazar T, Griffin J, Perry MS, Nascimento FA
1.376	Digital Health Technologies to Improve Health Outcomes for People Living With Epilepsy: A Scoping Review	Simic G, Fillios S, Hellier T, Vandenneucker J
1.377	Clinical and Economic Burden of Epilepsy According to the Number of Antiepileptic Drugs Received	Bénard M, Syed S, Aguilà Bargués M, Skornicki M, Ems D
1.378	Health Disparities in Black Patients Living With Epilepsy: Findings From a Survey of US Neurologists	Ebong I, Eads P, Charles G
1.387	Community Pharmacist-Centered Training Program Improves Confidence in Delivering Epilepsy Care	White HS, Guignet M, Novotny E, Stergachis A, Zaraa S, Nwogu IB, Ems D, Bacci J
1.435	Design of a Phase 3 Clinical Study to Examine the Safety, Effectiveness, and Pharmacokinetics of Fenfluramine in Infants with Dravet syndrome	Wheless J, Schoonjans A-S, Cleary E, Evans S, Morita D, Merazga Y
1.474	Systemic Exposure to Fenfluramine and its Active Metabolite Norfenfluramine in Patients With Lennox-Gastaut Syndrome	Mittur AM, Rubino C, Wheless J, Boyd B

Sunday, December 3, 2023 (12:00 PM –2:00 PM ET)

Poster number and title		**Authors**
2.254	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	Lagae L, Bourikas D, Dickson N, Dimova S, Elmoufti S, Moseley B, Kang H
2.255	Pulmonary Safety of **Staccato® Alprazolam in Healthy Participants and Participants with Mild Asthma: Phase 1, Randomized, Double-Blind, Placebo-Controlled Trial	Miller SD, LaForce CF, Barlow L, King A, Burian M, Chanteux H
2.261	Pharmacokinetics and Tolerability of Single-dose **Staccato® Alprazolam in Adolescents with Epilepsy and Population PK Analysis to Support Dose Selection in Adolescents	Klein P, Aungaroon G, Biton V, Liow KK, Phillips S, Wychowski T, Sadek A, Elshoff JP, Roebling R, King A, Ford A, Rospo CC, Schoemaker R, Chanteux H
2.262	Pharmacokinetics of **Staccato® Alprazolam in Healthy Adult Participants: Phase 1, Randomized, Placebo-Controlled Ethno-Bridging Study	Roebling R, Hayakawa Y, Rospo CC, Bartmann AP, King A, Chanteux H
2.267	Fenfluramine Increases Seizure-Free Days in Patients With Lennox-Gastaut Syndrome	Auvin S, Scheffer IE, Gil-Nagel A, Lothe A, Polega S, Lagae L, Knupp KG
2.270	Brivaracetam Adjunctive Therapy in Earlier Treatment Lines in Adults With Focal-Onset Seizures in Europe and Canada: Interim Results of 12-month Real-World Data from BRITOBA	Knake S, de Curtis M, Kobayashi E, Lema-Facal T, Maillard LG, Réhel B, Rheims S, Schulz AL, Leunikava I
2.271	Treatment Satisfaction, Work Productivity, and Quality of Life Under Adjunctive Brivaracetam in Earlier Treatment Lines in Adults With Focal-Onset Seizures: 6-Month Real-World Data from BRITOBA	Winter Y, Boero G, Didato G, Didelot A, Hirsch E, Kühn F, Navarro V, Réhel B, Schulz AL, Leunikava I
2.290	Pregnancy Outcomes Following Exposure to Lacosamide: Prospective Data From Spontaneous and Solicited Reports	Perucca P, Voinescu PE, Vadlamudi L, Bourikas D, Chellun D, Werhahn KJ, Kumke T, Schmitz B

2.376	Bridging The Gap Between Neurologists and People With Epilepsy/Caregivers: Systematic Literature Review About SUDEP Conversations	Ryvlin P, Stanton T, Shaw S, Mearns K, Luker J
2.445	Behavior and Executive Functioning During Adjunctive Brivaracetam Treatment of Pediatric Patients With Focal Seizures With or Without Cognitive or Learning Comorbidities	Bourikas D, Dickson N, de la Loge C, Dimova S, Elmoufti S, Moseley B, Lagae L
2.081	Seizure and Behavioral Phenotype in a Haploinsufficient Mouse Model with the Human SLC6A1 S295L Mutation Associated with Developmental and Epileptic Encephalopathy	Van Den Herrewegen Y, Clasadonte J, Rodriguez N, Lugara E, Goursaud E, Gillent E, Bonnaillie P, Mairet-Coello G, Widya M, Vandenplas C, Wolff C, Vallette B, Dedeurwaerdere S

Monday, December 4, 2023 (12:00 PM –1:45 PM ET)

Poster number and title		**Authors**
3.277	Descriptive Analysis of Fenfluramine Use in Adult Patients With Dravet Syndrome Enrolled in an Open-Label Extension Study	Sánchez-Carpintero R, Devinsky O, Gil-Nagel A, Morita D, Langlois M, Lothe A, Polega S, Jacobs-Le Van J, Scheffer IE, Healy P
3.294	Modeling Systemic Exposure to Fenfluramine and its Active Metabolite, Norfenfluramine, in Patients with Dravet Syndrome	Mittur AM, Rubino C, Auvin S, Specchio N, Boyd B
3.490	A 12-Month Persistence Analysis of Fenfluramine, Valproate, and Levetiracetam in Individuals with Dravet Syndrome: A Comparison Using US Claims Data	Jaganathan S, Ems D, Sederman R, Chen C, Wu S
3.021	A longitudinal Monitoring of Neurobehaviors and Brain GABA Concentration in Slc6a1+/S295L and Slc6a1+/A288V Mouse Models Associated with Developmental Epileptic Encephalopathies.	Randhave K, Clasadonte J, Biven M, Zavalin K, Paffenroth K, Allison J, Shen W, Khan M, Harrison F, Dedeurwaerdere S, Kang J

*The Seizure Termination Project was funded by UCB Pharma.

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

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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 8,600 people in approximately 40 countries, the company generated revenue of €5.5 billion in 2022. 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 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

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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; 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 co-administration with a strong CYP1A2 or CYP2D6 inhibitor may result in higher exposure (see section 4.4 of the SmPC). Co-administration 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]

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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 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 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

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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 CYP-independent 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 C_{max} 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 co-administered 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 post-marketing experience. In general, the adverse reactions associated with brivaracetam overdose were consistent with the known adverse reactions. There is no specific 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

Important Safety Information about VIMPAT® (lacosamide) in the EU[3]

Therapeutic indications: VIMPAT® is indicated as monotherapy in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 2 years of age with epilepsy. VIMPAT® 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 and in the treatment of primary generalised tonic-clonic seizures in adults, adolescents and children from 4 years of age with idiopathic generalised epilepsy.

Posology and method of administration: Lacosamide therapy can be initiated with either oral administration (either tablets or syrup) or IV administration (solution for infusion). The physician should prescribe the most appropriate formulation and strength according to weight and dose. A loading dose may be initiated in patients in situations when the physician determines that rapid attainment of lacosamide steady state plasma concentration and therapeutic effect is warranted. It should be administered under medical supervision with consideration of the potential for increased incidence of serious cardiac arrhythmia and Central Nervous System (CNS) adverse reactions. Administration of a loading dose has not been studied in acute conditions such as status epilepticus. Administration of a loading dose has not been studied in children. Use of a loading dose is not recommended in adolescents and children weighing less than 50 kg. No dose adjustment is necessary in mildly and moderately renally impaired adult and paediatric patients (CLCR > 30 ml/min). In paediatric patients weighing 50 kg or more and in adult patients with mild or moderate renal impairment, a loading dose of 200 mg may be considered, but further dose titration (>200 mg daily) should be performed with caution. In paediatric patients weighing 50 kg or more and in adult patients with severe renal impairment (CLCR ≤ 30 ml/min) or with end-stage renal disease, a maximum dose of 250 mg/day is recommended and the dose titration should be performed with caution. In paediatric patients weighing less than 50 kg with severe renal impairment (CLCR ≤ 30 ml/min) and in those with end-stage renal disease, a reduction of 25 % of the maximum dose is recommended. A maximum dose of 300 mg/day is recommended for paediatric patients weighing 50 kg or more and for adult patients with mild to moderate hepatic impairment. Based on data in adults, in paediatric patients weighing less than 50 kg with mild to moderate hepatic impairment, a reduction of 25 % of the maximum dose should be applied. Lacosamide should be administered to adult and paediatric patients with severe hepatic impairment only when the expected therapeutic benefits are anticipated to outweigh the possible risks. The dose may need to be adjusted while carefully observing disease activity and potential side effects in the patient. In adolescents and adults weighing 50 kg or more with mild to moderate hepatic impairment a loading dose of 200mg may be considered, but further dose titration (>200 mg daily) should be performed with caution. Lacosamide is not recommended for use in children below the age of 4 years in the treatment of primary generalized tonic-clonic seizures and below the age of 2 years in the treatment of partial-onset seizures as there are limited data on safety and efficacy in these age groups. **Contraindications:** Hypersensitivity to the active substance or any of the excipients; known second- or third-degree atrioventricular (AV) block. **Special warnings and precautions for use:** Suicidal ideation and behaviour have been reported in patients treated with antiepileptic medicinal products in several indications. Therefore, patients should be monitored for signs of suicidal ideation and behaviour 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. Dose-related prolongations in PR interval with lacosamide have been observed in clinical studies. Lacosamide should be used with caution in patients with underlying proarrhythmic conditions such as known cardiac conduction problems or severe cardiac diseases (e.g. myocardial ischaemia/infarction, heart failure, structural heart disease or cardiac sodium channelopathies) or patients treated with medicinal products affecting cardiac conduction, including antiarrhythmics and sodium channel blocking antiepileptic medicinal products, as well as in elderly patients. In these patients it should be considered to perform an electrocardiogram (ECG) before a lacosamide dose increase above 400mg/day

Date of preparation: November 2023
GL-BR-2300007

and after lacosamide is titrated to steady-state. In the placebo-controlled clinical studies of lacosamide in epilepsy patients, atrial fibrillation or flutter were not reported; however both have been reported in open-label epilepsy studies and in post-marketing experience. In post-marketing experience, AV block (including second degree or higher AV block) has been reported. In patients with proarrhythmic conditions, ventricular tachyarrhythmia has been reported. In rare cases, these events have led to asystole, cardiac arrest and death in patients with underlying proarrhythmic conditions. Patients should be made aware of the symptoms of cardiac arrhythmia (e.g. slow, rapid or irregular pulse, palpitations, shortness of breath, feeling lightheaded, fainting). Patients should be counselled to seek immediate medical advice if these symptoms occur. 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. New onset or worsening of myoclonic seizures has been reported in both adult and paediatric patients with primary generalized tonic-clonic seizures (PGTCS), in particular during titration. In patients with more than one seizure type, the observed benefit of control for one seizure type should be weighed against any observed worsening in another seizure type. The safety and efficacy of lacosamide in paediatric patients with epilepsy syndromes in which focal and generalised seizures may coexist have not been determined. VIMPAT® syrup contains sodium methyl parahydroxybenzoate (E219) which may cause allergic reactions (possibly delayed). Vimpat Syrup contains sorbitol (E420). Patients with rare hereditary problems of fructose intolerance should not take this medicine. Sorbitol may cause gastrointestinal discomfort and mild laxative effect. The syrup contains aspartame (E951), a source of phenylalanine, which may be harmful for people with phenylketonuria. Neither non-clinical nor clinical data are available to assess aspartame use in infants below 12 weeks of age. Vimpat syrup contains propylene glycol (E1520). VIMPAT® syrup contains 1.42 mg sodium per ml, equivalent to 0.07 % of the WHO recommended maximum daily intake of 2 g sodium for an adult. VIMPAT® solution for infusion contains 59.8 mg sodium per vial, equivalent to 3% of the WHO recommended maximum daily intake of 2 g sodium for an adult. **Effects on ability to drive and use machines**: Lacosamide may have minor to moderate influence on the ability to drive and use machines. Lacosamide treatment has been associated with dizziness or blurred vision. Accordingly, patients should be advised not to drive a car or to operate other potentially hazardous machinery until they are familiar with the effects of lacosamide on their ability to perform such activities. **Undesirable effects:** The most frequently reported adverse reactions (≥10%) are dizziness, headache, nausea and diplopia. They were usually mild to moderate in intensity. Some were dose-related and could be alleviated by reducing the dose. Incidence and severity of CNS and gastrointestinal (GI) adverse reactions usually decreased over time. Incidence of CNS adverse reactions such as dizziness may be higher after a loading dose. Other common adverse reactions (≥1% - <10%) are depression, confusional state, insomnia, balance disorder, myoclonic seizures, ataxia, memory impairment, cognitive disorder, somnolence, tremor, nystagmus, hypoesthesia, dysarthria, disturbance in attention, paraesthesia, vision blurred, vertigo, tinnitus, vomiting, constipation, flatulence, dyspepsia, dry mouth, diarrhoea, pruritus, rash, muscle spasms, gait disturbance, asthenia, fatigue, irritability, feeling drunk, injection site pain or discomfort (local adverse events associated with intravenous administration), irritation (local adverse events associated with intravenous administration), fall, and skin laceration and contusion. The use of lacosamide is associated with dose-related increase in the PR interval. Adverse reactions associated with PR interval prolongation (e.g. atrioventricular block, syncope, bradycardia) may occur. Multiorgan Hypersensitivity **Reactions**: Multiorgan hypersensitivity reactions (also known as Drug Reaction with Eosinophilia and Systemic Symptoms, DRESS) have been reported in patients treated with some antiepileptic medicinal products. These reactions are variable in expression but typically present with fever and rash and can be associated with involvement of different organ systems. If multiorgan hypersensitivity reaction is suspected, lacosamide should be discontinued. The safety profile of lacosamide in adjunctive therapy in paediatric patients with partial-onset seizures was consistent with the safety profile observed in adults. The additional adverse reactions observed in the paediatric population were pyrexia, nasopharyngitis, pharyngitis, decreased appetite, abnormal behaviour and lethargy. Somnolence was reported more frequently in the paediatric population (≥ 1/10) compared to the adult population (≥ 1/100 to < 1/10).

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/vimpat-epar-product-information_en.pdf

Important Safety Information about FINTEPLA® (fenfluramine) in the US[4]

FINTEPLA is indicated for the treatment of seizures associated with Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS) in patients 2 years of age and older.

FINTEPLA is available only through a restricted distribution program called the FINTEPLA REMS. Further information is available at www.FinteplaREMS.com or by telephone at +1 877 964 3649.
IMPORTANT SAFETY INFORMATION

BOXED WARNING: VALVULAR HEART DISEASE and PULMONARY ARTERIAL HYPERTENSION

- There is an association between serotonergic drugs with 5-HT2B receptor agonist activity, including fenfluramine (the active ingredient in FINTEPLA), and valvular heart disease and pulmonary arterial hypertension.

Date of preparation: November 2023
GL-BR-2300007

- Echocardiogram assessments are required before, during, and after treatment with FINTEPLA.
- FINTEPLA is available only through a restricted program called the FINTEPLA REMS.

CONTRAINDICATIONS
FINTEPLA is contraindicated in patients with hypersensitivity to fenfluramine or any of the excipients in FINTEPLA and with concomitant use, or within 14 days of the administration, of monoamine oxidase inhibitors because of an increased risk of serotonin syndrome.

WARNINGS AND PRECAUTIONS

Valvular Heart Disease and Pulmonary Arterial Hypertension (see Boxed Warning): Because of the association between serotonergic drugs with 5-HT2B receptor agonist activity, including fenfluramine (the active ingredient in FINTEPLA), and valvular heart disease (VHD) and pulmonary arterial hypertension (PAH), cardiac monitoring via echocardiogram is required prior to starting treatment, during treatment, and after treatment with FINTEPLA concludes. Cardiac monitoring via echocardiogram can aid in early detection of these conditions. In clinical trials for DS and LGS of up to 3 years in duration, no patient receiving FINTEPLA developed VHD or PAH.

Monitoring: Prior to starting treatment, patients must undergo an echocardiogram to evaluate for VHD and PAH. Echocardiograms should be repeated every 6 months, and once at 3-6 months post treatment with FINTEPLA.

The prescriber must consider the benefits versus the risks of initiating or continuing treatment with FINTEPLA if any of the following signs are observed via echocardiogram: valvular abnormality or new abnormality; VHD indicated by mild or greater aortic regurgitation or moderate or greater mitral regurgitation, with additional characteristics of VHD (eg, valve thickening or restrictive valve motion); PAH indicated by elevated right heart/pulmonary artery pressure (PASP >35 mmHg).

FINTEPLA REMS Program (see Boxed Warning): FINTEPLA is available only through a restricted distribution program called the FINTEPLA Risk Evaluation and Mitigation Strategy (REMS) Program. Prescribers must be certified by enrolling in the FINTEPLA REMS. Prescribers must counsel patients receiving FINTEPLA about the risk of VHD and PAH, how to recognize signs and symptoms of VHD and PAH, the need for baseline (pretreatment) and periodic cardiac monitoring via echocardiogram during FINTEPLA treatment, and cardiac monitoring after FINTEPLA treatment. Patients must enroll in the FINTEPLA REMS and comply with ongoing monitoring requirements. The pharmacy must be certified by enrolling in the FINTEPLA REMS and must only dispense to patients who are authorized to receive FINTEPLA. Wholesalers and distributors must only distribute to certified pharmacies. Further information is available at www.FinteplaREMS.com or by telephone at 1-877-964-3649.

Decreased Appetite and Decreased Weight: FINTEPLA can cause decreases in appetite and weight. Decreases in weight appear to be dose related. Approximately half of the patients with LGS and most patients with DS resumed the expected measured increases in weight during the open-label extension studies. Weight should be monitored regularly during treatment with FINTEPLA, and dose modifications should be considered if a decrease in weight is observed.

Somnolence, Sedation, and Lethargy: FINTEPLA can cause somnolence, sedation, and lethargy. Other central nervous system (CNS) depressants, including alcohol, could potentiate these effects of FINTEPLA. Prescribers should monitor patients for somnolence and sedation and should advise patients not to drive or operate machinery until they have gained sufficient experience on FINTEPLA to gauge whether it adversely affects their ability to drive or operate machinery.

Suicidal Behavior and Ideation: Antiepileptic drugs (AEDs), including FINTEPLA, increase the risk of suicidal thoughts or behaviors in patients taking these drugs for any indication. Patients treated with an AED for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behaviors, or any unusual changes in mood or behavior.

Anyone considering prescribing FINTEPLA or any other AED must balance the risk of suicidal thoughts or behaviors with the risks of untreated illness. Epilepsy and many other illnesses for which AEDs are prescribed are themselves associated with morbidity and mortality and an increased risk of suicidal thoughts and behaviors. Should suicidal thoughts and behaviors emerge during treatment, consider whether the emergence of these symptoms in any given patient may be related to the illness being treated.

Withdrawal of Antiepileptic Drugs: As with most AEDs, FINTEPLA should generally be withdrawn gradually because of the risk of increased seizure frequency and status epilepticus. If withdrawal is needed because of a serious adverse reaction, rapid discontinuation can be considered.

Date of preparation: November 2023
GL-BR-2300007

Serotonin Syndrome: Serotonin syndrome, a potentially life-threatening condition, may occur with FINTEPLA, particularly during concomitant administration of FINTEPLA with other serotonergic drugs, including, but not limited to, selective serotonin-norepinephrine reuptake inhibitors (SNRIs), selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), bupropion, triptans, dietary supplements (eg, St. John's Wort, tryptophan), drugs that impair metabolism of serotonin (including monoamine oxidase inhibitors [MAOIs], which are contraindicated with FINTEPLA), dextromethorphan, lithium, tramadol, and antipsychotics with serotonergic agonist activity. Patients should be monitored for the emergence of signs and symptoms of serotonin syndrome, which include mental status changes (eg, agitation, hallucinations, coma), autonomic instability (eg, tachycardia, labile blood pressure, hyperthermia), neuromuscular signs (eg, hyperreflexia, incoordination), and/or gastrointestinal symptoms (eg, nausea, vomiting, diarrhea). If serotonin syndrome is suspected, treatment with FINTEPLA should be stopped immediately and symptomatic treatment should be started.

Increase in Blood Pressure: FINTEPLA can cause an increase in blood pressure. Rare cases of significant elevation in blood pressure, including hypertensive crisis, has been reported in adult patients treated with fenfluramine, including patients without a history of hypertension. In clinical trials for DS and LGS of up to 3 years in duration, no pediatric or adult patient receiving FINTEPLA developed hypertensive crisis. Monitor blood pressure in patients treated with FINTEPLA.

Glaucoma: Fenfluramine can cause mydriasis and can precipitate angle closure glaucoma. Consider discontinuing treatment with FINTEPLA in patients with acute decreases in visual acuity or ocular pain.

ADVERSE REACTIONS
The most common adverse reactions observed in DS studies (incidence at least 10% and greater than placebo) were decreased appetite; somnolence, sedation, lethargy; diarrhea; constipation; abnormal echocardiogram; fatigue, malaise, asthenia; ataxia, balance disorder, gait disturbance; blood pressure increased; drooling, salivary hypersecretion; pyrexia; upper respiratory tract infection; vomiting; decreased weight; fall; status epilepticus.

The most common adverse reactions observed in the LGS study (incidence at least 10% and greater than placebo) were diarrhea; decreased appetite; fatigue; somnolence; vomiting.

DRUG INTERACTIONS
Strong CYP1A2, CYP2B6, or CYP3A Inducers: Coadministration with strong CYP1A2, CYP2B6, or CYP3A inducers will decrease fenfluramine plasma concentrations. If coadministration of a strong CYP1A2, CYP2B6, or CYP3A inducer with FINTEPLA is necessary, monitor the patient for reduced efficacy and consider increasing the dosage of FINTEPLA as needed. If a strong CYP1A2, CYP2B6, or CYP3A inducer is discontinued during maintenance treatment with FINTEPLA, consider gradual reduction in the FINTEPLA dosage to the dose administered prior to initiating the inducer.

Strong CYP1A2 or CYP2D6 Inhibitors: Coadministration with strong CYP1A2 or CYP2D6 inhibitors will increase fenfluramine plasma concentrations. If FINTEPLA is coadministered with strong CYP1A2 or CYP2D6 inhibitors, the maximum daily dosage of FINTEPLA is 20 mg. If a strong CYP1A2 or CYP2D6 inhibitor is discontinued during maintenance treatment with FINTEPLA, consider gradual increase in the FINTEPLA dosage to the dose recommended without CYP1A2 or CYP2D6 inhibitors. If FINTEPLA is coadministered with stiripentol and a strong CYP1A2 or CYP2D6 inhibitor, the maximum daily dosage of FINTEPLA is 17 mg.

USE IN SPECIFIC POPULATIONS
In patients with severe impairment of kidney function (estimated glomerular filtration rate [eGFR]) 15 to 29 mL/min/1.73m^2, dosage adjustments are recommended. FINTEPLA has not been studied in patients with kidney failure (eGFR <15 mL/min/1.73m^2). Combined molar exposures of fenfluramine and norfenfluramine were increased in subjects with various degrees of hepatic impairment (Child-Pugh Class A, B, and C), necessitating a dosage adjustment in these patients.

To report SUSPECTED ADVERSE REACTIONS, contact UCB, Inc. at 1-844-599-2273 or FDA at 1-800-FDA-1088 or **www.fda.gov/medwatch**.

Please see full Prescribing Information, including Boxed Warning and Medication Guide, for additional Important Safety Information on FINTEPLA.

Important Safety Information about BRIVIACT® (brivaracetam) in the US[5]

BRIVIACT® (brivaracetam) CV is indicated for the treatment of partial-onset seizures in patients 1 month of age and

Date of preparation: November 2023
GL-BR-2300007

older.

WARNINGS AND PRECAUTIONS

Suicidal Behavior and Ideation: Antiepileptic 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. 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 in adult and pediatric patients. 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 Antiepileptic Drugs: As with all antiepileptic 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 were generally similar to those in adult patients. Adverse reactions with BRIVIACT injection in adult and pediatric patients were generally similar to those observed with BRIVIACT tablets. Other adverse events that occurred in adult patients who received BRIVIACT injection included dysgeusia, euphoric mood, feeling drunk, and infusion site pain.

BRIVIACT is a Schedule V controlled substance.

Please refer to the full Prescribing Information and visit www.BRIVIACThcp.com.

Important Safety Information about VIMPAT® (lacosamide) in the US[6]

VIMPAT® is indicated for treatment of partial-onset seizures in patients 1 month of age and older, and as adjunctive therapy in the treatment of primary generalized tonic-clonic seizures in patients 4 years of age and older.

VIMPAT IMPORTANT SAFETY INFORMATION
VIMPAT® is indicated for the treatment of partial-onset seizures in patients 1 month of age and older. VIMPAT is indicated as adjunctive therapy in the treatment of primary generalized tonic-clonic seizures in patients 4 years of age and older.
VIMPAT is associated with important warnings and precautions including suicidal behavior and ideation, dizziness and ataxia, cardiac rhythm and conduction abnormalities, syncope, and Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), also known as multi-organ hypersensitivity.

Partial-Onset Seizures
In the adult adjunctive placebo-controlled trials for partial-onset seizures, the most common adverse reactions (≥10% and greater than placebo) were dizziness, headache, nausea, and diplopia. In the adult monotherapy clinical trial, adverse reactions were generally

Date of preparation: November 2023
GL-BR-2300007

similar to those observed and attributed to drug in adjunctive placebo-controlled trials, with the exception of insomnia (observed at a higher rate of ≥2%).

Primary Generalized Tonic-Clonic Seizures
In the adjunctive therapy placebo-controlled trial for primary generalized tonic-clonic seizures, the adverse reactions were generally similar to those that occurred in the partial-onset seizures trials. The adverse reactions most commonly reported were dizziness, somnolence, headache, and nausea.

Pediatric Patients
Adverse reactions reported in clinical studies for partial-onset seizures in patients 1 month to less than 17 years of age and for primary generalized tonic-clonic seizures for patients 4 to less than 17 years of age were similar to those seen in adult patients.

Injection
In adult adjunctive therapy clinical trials for partial-onset seizures, adverse reactions with intravenous administration generally were similar to those that occurred with the oral formulation, although intravenous administration was associated with local adverse reactions such as injection site pain or discomfort (2.5%), irritation (1%), and erythema (0.5%). When administering a loading dose, the incidence of CNS adverse reactions, such as dizziness, somnolence, and paresthesia, may be higher with 15-minute administration than over a 30- to 60-minute period. The adverse reactions associated with VIMPAT injection in adult patients with primary generalized tonic-clonic seizures are expected to be similar to those seen in adults with partial- onset seizures. The adverse reactions associated with VIMPAT injection in pediatric patients are expected to be similar to those noted in adults. Infusion times less than 30 minutes were not adequately studied in pediatric patients.

VIMPAT (lacosamide) is a Schedule V controlled substance.
Please refer to the full Prescribing Information.

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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 pressure, political and public scrutiny, customer and prescriber patterns or practices, and the reimbursement policies imposed by third-party payers as well as legislation affecting biopharmaceutical pricing and reimbursement activities and outcomes. Finally, a breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of UCB's data and systems.

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