UCB News

UCB Showcases Strength and Depth of Neurology Portfolio at 75th American Academy of Neurology (AAN) Annual Meeting

- New insights from leading portfolio demonstrate ongoing commitment to improving outcomes and experiences of those living with epilepsy and rare epileptic syndromes
- Data will showcase further insights into the potential of UCB's generalized myasthenia gravis (gMG) pipeline
- UCB will also host an industry sponsored therapeutic update session on recognizing and treating seizure emergencies in adults and on the identification of seizure clusters through relevant patient cases

Brussels, Belgium, 20 April 2023 – 7:00 AM CET – UCB will showcase data from its expansive and innovative neurology portfolio at the 75th American Academy of Neurology (AAN) Annual Meeting, April 22-27, 2023. The company will present 12 abstracts, including two oral presentations, across generalized myasthenia gravis (gMG), Lennox-Gastaut syndrome (LGS), and focal (partial) epileptic seizures.

Presentations of clinical and real-world evidence will offer new insights about the efficacy and safety profile of BRIVIACT® (brivaracetam) CV in multiple age groups, as well as the efficacy and safety profile of FINTEPLA® (fenfluramine) on seizure and non-seizure parameters, such as everyday executive functioning, in children and adults living with LGS.

In gMG, presentations will expand on the results from the MycarinG and RAISE studies[1,2]. These pivotal Phase 3 trials supported the U.S., European and Japanese regulatory filings of two investigational treatments with different modes of action, rozanolixizumab and zilucoplan, for the treatment of gMG in adults. Rozanolixizumab is a subcutaneously (SC) infused monoclonal antibody targeting the neonatal Fc receptor (FcRn), and zilucoplan is a daily self-injected SC peptide inhibitor of complement component 5 (C5 inhibitor)[3,4,5]. The data further informs UCB's innovative approach to developing scientific solutions that may help improve outcomes and address unmet needs of people living with gMG. The safety and efficacy of rozanolixizumab and zilucoplan have not been established and they are not currently approved for use in any indication by any regulatory authority worldwide.

Charl van Zyl, Executive Vice President Neurology and Head of EU/International Markets, UCB, said: "Our presentations at AAN reinforce the strength and depth of our expanding rare disease pipeline and portfolio. This is an exciting year for UCB, as we further deliver on our ambition and commitment to improving the outcomes and experiences of people living with severe neurological disorders."

Symposium Focus on Seizure Clusters in Adult Populations
Seizure Clusters Identification in Adults: An Interactive Case-Based Approach – Saturday, April 22, 2023 (11:45 AM – 12:45 PM ET); Room 052B, Boston Convention and Exhibitor Center, 415 Summer Street, Boston, MA. An interactive case-based lunch symposium where epilepsy experts will discuss seizure emergencies and the identification of seizure clusters through relevant patient cases. This session will

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focus on recognizing and treating seizure emergencies in the adult population. Esteemed speakers include: Kamil Detyniecki, MD; Steve Chung, MD; Sheryl Haut, MD.

UCB Presentations During AAN 2023

Lead Author	Abstract title	Presentation Details (Timings ET)
gMG		
Bril V	Long-term efficacy and safety of symptom-driven cyclic rozanolixizumab treatment in patients with generalized Myasthenia Gravis: A pooled analysis of a phase 3 study and two open-label extension studies	Poster Presentation P1: 012 April 23, 2023 8:00 – 9:00 AM
Weiss M	Subgroup outcomes from RAISE: A randomized, phase 3 trial of zilucoplan in generalized Myasthenia Gravis	Poster Presentation P1: 006 April 23, 2023 8:00 – 9:00 AM
Freimer M	RAISE-XT: An interim analysis of safety and efficacy in an open-label extension study of zilucoplan in patients with Myasthenia Gravis	Poster Presentation P1: 007 April 23, 2023 8:00 – 9:00 AM
Vu T	Efficacy of rozanolixizumab in generalized Myasthenia Gravis: Subgroup analyses from the randomized phase 3 MycarinG study	Oral Presentation S5: 007 April 23, 2023 2:12 PM
Epilepsy & Rare Epileptic Syndromes		
Knupp KG	Impact of fenfluramine on drop seizure frequency in adults or dose-capped patients with Lennox-Gastaut syndrome: Comparative analysis of clinical trial data	Oral Presentation S44: 002 April 27, 2023 1:12 PM
Cross H	Effect of fenfluramine on Generalized Tonic-Clonic Seizures in rare epilepsy syndromes: a review of published studies	Poster Presentation P3: 010 April 23, 2023 5:30 – 6:30 PM
Peeples H	Access to neurology healthcare professionals in the United States among Medicaid patients with epilepsy	Poster Presentation P6: 009 April 24, 2023 5:30 – 6:30 PM
Martin L	Effectiveness and tolerability of brivaracetam by number of lifetime antiseizure medications in adults with focal onset seizures: Pooled data from two real-world studies	Poster Presentation P:11 010 April 26, 2023 11:45 AM – 12:45 PM
Villanueva V	12-month effectiveness and tolerability of brivaracetam in the real-world: The international EXPERIENCE pooled analysis	Poster Presentation P:11 003 April 26, 2023 11:45 AM – 12:45 PM
Bishop KI	Fenfluramine treatment is associated with improvement in everyday executive function in adults with Lennox-Gastaut	Poster Presentation P11: 001

	syndrome: Post hoc analysis of dose effects from a phase 3 trial rationale	April 26, 2023 11:45 AM – 12:45 PM
Elshoff JP	Cognitive and behavioral effects of adjunctive brivaracetam in children and adolescents with focal seizures: Final data from an open-label follow-up trial	Poster presentation P14: 007 April 27, 2023 11:45 AM – 12:45 PM
Dave H	Treatment outcomes during brivaracetam treatment by seizure freedom status: Post hoc analysis of a real-world, US study	Poster Presentation P14: 001 April 27, 2023 11:45 AM – 12:45 PM

About BRIVIACT® (brivaracetam) in the EU[6]

Important Safety Information about BRIVIACT in the EU[6]

BRIVIACT (brivaracetam) 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. **Contraindications** Hypersensitivity to the active substance, other pyrrolidone derivatives or any of the excipients. **Special warnings and precautions for use** Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic drugs (AEDs) in several indications, including BRIVIACT. Patients should be monitored for signs of suicidal ideation and behaviour and appropriate treatment should be considered. Patients (and caregivers) should be advised to seek medical advice should any signs of suicidal ideation or behaviour emerge. BRIVIACT film-coated tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take BRIVIACT. 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'. The 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). **Posology** No dose adjustment is needed in adults with impaired renal function. Based on data in adults, no dose adjustment is necessary neither in paediatric patients with impaired renal function. No clinical data are available in paediatric patients with renal impairment. 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 starting dose 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 starting dose is recommended, with a maximum daily dose of 4 mg/kg/day. No clinical data are available in paediatric patients with hepatic impairment. **Interaction with other medicinal products and other forms of interaction.** With co-administration of BRIVIACT 200 mg single dose and ethanol 0.6 g/L continuous infusion in healthy subjects there was no pharmacokinetic interaction, but the effect of alcohol on psychomotor function, attention and memory was doubled. Intake of BRIVIACT with alcohol is not recommended. 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 rifampicin, a strong enzyme-inducer (600 mg/day for 5 days), decreased BRIVIACT area under the plasma concentration curve (AUC) by 45%. Prescribers should consider adjusting the dose of BRIVIACT for patients starting or ending treatment with rifampicin. Other strong enzyme-inducers (such as St Johns wort [Hypericum perforatum]) may also decrease the systemic exposure of BRIVIACT. Therefore, starting or ending treatment with St John's wort should be done with caution. *In vitro* studies have shown that brivaracetam exhibits little or no inhibition of CYP450 isoforms except for CYP2C19. Brivaracetam may increase plasma concentrations of medicinal products metabolised by CYP2C19 (e.g., lansoprazole, omeprazole, diazepam). CYP2B6 induction has not been investigated in vivo and BRIVIACT may decrease plasma concentrations of medicinal products metabolised by CYP2B6 (e.g. efavirenz). In vitro studies have also shown that BRIVIACT has inhibitory effects on OAT3. BRIVIACT 200 mg/day may increase plasma concentrations of medicinal products transported by OAT3. BRIVIACT plasma concentrations are decreased when co-administered with strong enzyme inducing antiepileptic drugs (carbamazepine, phenobarbital, phenytoin) but no dose adjustment is required. **Effects on ability to drive and use machines** BRIVIACT, has minor or moderate influence on the ability to drive and use machines. Patients should be advised not to drive a car or

to operate other potentially hazardous machines until they are familiar with the effects of BRIVIACT, on their ability to perform such activities. **Undesirable effects.** The most frequently reported adverse reactions with BRIVIACT (reported by >10% of patients) were somnolence (14.3%) and dizziness (11.0%). They were usually mild to moderate in intensity. Somnolence and fatigue were reported at higher incidences with increasing dose. Very common adverse reactions (≥1% to <10%) were influenza, decreased appetite, depression, anxiety, insomnia, irritability, convulsion, vertigo, upper respiratory tract infections, cough, nausea, vomiting, constipation and fatigue. Neutropenia has been reported in 0.5% (6/1,099) BRIVIACT patients and 0% (0/459) placebo-treated patients. Four of these patients had decreased neutrophil counts at baseline, and experienced additional decrease in neutrophil counts after initiation of BRIVIACT. None of the six cases were severe, required any specific treatment, led to BRIVIACT discontinuation, or had associated infections. Suicidal ideation was reported in 0.3 % (3/1099) of BRIVIACT treated patients and 0.7 % (3/459) of placebo-treated patients. In short-term clinical studies of BRIVIACT in patients with epilepsy, there were no cases of completed suicide and suicide attempt, however both were reported in the long-term open-label extension studies. Reactions suggestive of immediate (Type I) hypersensitivity have been reported in a small number of BRIVIACT patients (9/3022) during clinical development. 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. No clinical data are available in neonates. **Overdose** There is limited clinical experience with BRIVIACT overdose in humans. Somnolence and dizziness were reported in a healthy subject taking a single dose of 1,400 mg of BRIVIACT. 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. Treatment of an overdose should include general supportive measures. Since less than 10% of BRIVIACT is excreted in urine, haemodialysis is not expected to significantly enhance BRIVIACT clearance.

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

About BRIVIACT® (brivaracetam) CV in the U.S.[7]

BRIVIACT is indicated for the treatment of partial-onset seizures in patients 1 month of age and older. BRIVIACT is available in three formulations: oral tablets, oral solution, and intravenous (IV) injection. More information is available at Drugs@FDA: FDA-Approved Drugs.

BRIVIACT IMPORTANT SAFETY INFORMATION (U.S.)

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.

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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.

About FINTEPLA®▼(fenfluramine) oral solution in EU[8]

FINTEPLA is indicated for the treatment of seizures associated with Lennox-Gastaut and Dravet syndrome as an add-on therapy to other anti-epileptic medicines for patients 2 years of age and older. Fenfluramine is a serotonin releasing agent, and thereby stimulates multiple 5-HT receptor sub-types through the release of serotonin. Fenfluramine may reduce seizures by acting as an agonist at specific serotonin receptors in the brain, including the 5-HT1D, 5-HT2A, and 5-HT2C receptors, and also by acting on the sigma-1 receptor. The precise mode of action of fenfluramine in Dravet syndrome and Lennox-Gastaut syndrome is not known.

Fenfluramine oral solution is available under a controlled access program to ensure regular cardiac monitoring and to mitigate potential off-label use.

Please refer to Fintepla, INN-fenfluramine (europa.eu) (SmPC) before prescribing.

▼*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.*

Important Safety Information about FINTEPLA®▼ in EU[8]

Aortic or mitral valvular heart disease and pulmonary arterial hypertension
Because of reported cases of valvular heart disease that may have been caused by fenfluramine at higher doses used to treat adult obesity, cardiac monitoring must be performed using echocardiography. In the controlled clinical studies of fenfluramine for the treatment of Dravet syndrome and Lennox-Gastaut syndrome, no valvular heart disease was observed. Prior to starting treatment, patients must undergo an echocardiogram to establish a baseline prior to initiating treatment and exclude any pre-existing valvular heart disease or pulmonary hypertension. Echocardiogram monitoring should be conducted every 6 months for the first 2 years and annually thereafter. If an echocardiogram indicates pathological valvular changes, a follow-up echocardiogram should be considered at an earlier timeframe to evaluate whether the abnormality is persistent. If pathological abnormalities on the echocardiogram are observed, it is recommended to evaluate the benefit versus risk of continuing fenfluramine treatment with the prescriber, caregiver, and cardiologist. If treatment is stopped because of aortic or mitral valvular heart disease, appropriate monitoring and follow-up should be provided in accordance with local guidelines for the treatment of aortic or mitral valvular heart disease. With past use in higher doses to treat adult obesity, fenfluramine was reported to be associated with pulmonary arterial hypertension. Pulmonary arterial hypertension was not observed in the clinical programme, but because of the low incidence of this disease, the clinical trial experience with fenfluramine is inadequate to determine if fenfluramine increases the risk for pulmonary arterial hypertension in patients with Dravet syndrome and Lennox-Gastaut syndrome. If echocardiogram findings are suggestive of pulmonary arterial hypertension, a repeat echocardiogram should be performed as soon as possible and within 3 months to confirm these findings. If the echocardiogram finding is confirmed suggestive of an increased probability of pulmonary arterial hypertension defined as "intermediate probability" by the 2015 European Society of Cardiology (ESC) and the European Respiratory Society (ERS) Guidelines, it should lead to a benefit-risk evaluation of continuation of Fintepla by the prescriber, carer, and cardiologist. If the echocardiogram finding, after confirmation, suggests of a high probability of pulmonary arterial hypertension, as defined by the 2015 ESC and ERS Guidelines, it is recommended fenfluramine treatment should be stopped.

Decreased appetite and weight loss
Fenfluramine can cause decreased appetite and weight loss. An additive effect on decreased appetite can occur when fenfluramine is combined with other anti-epileptic medicines, for example stiripentol. The decrease in weight appears to be dose related. Most subjects resumed weight gain over time while continuing treatment. The patient's weight should be monitored. A benefit risk evaluation should be undertaken prior to commencing treatment with fenfluramine in patients with a history of anorexia nervosa or bulimia nervosa.

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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. Other central nervous system depressants, including alcohol, could potentiate the somnolence effect of fenfluramine.

Suicidal behaviour and ideation
Suicidal behaviour and ideation have been reported in patients treated with anti-epileptic medicines in several indications. A meta-analysis of randomised placebo-controlled trials with anti-epileptic medicines that did not include fenfluramine has shown a small increased risk of suicidal behaviour and ideation. The mechanism of this risk is not known, and the available data do not exclude the possibility of an increased risk for fenfluramine. Patients and caregivers of patients should be advised to seek medical advice should any signs of suicidal behaviour and ideation emerge.

Serotonin syndrome
As with other serotonergic agents, serotonin syndrome, a potentially life-threatening condition, may occur with fenfluramine treatment, particularly with concomitant use of other serotonergic agents (including SSRIs, SNRIs, tricyclic antidepressants, or triptans); with agents that impair metabolism of serotonin such as MAOIs; or with antipsychotics that may affect the serotonergic neurotransmitter systems. Serotonin syndrome symptoms may include mental status changes (eg, agitation, hallucinations, coma), autonomic instability (eg, tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (eg, hyperreflexia, incoordination), and/or gastrointestinal symptoms (eg, nausea, vomiting, diarrhoea). If concomitant treatment with fenfluramine and other serotonergic agents that may affect the serotonergic systems is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases.

Increased seizure frequency
As with other anti-epileptic medicines, a clinically relevant increase in seizure frequency may occur during treatment with fenfluramine, 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, patients should be monitored 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 there is ocular pain and another cause cannot be determined.

Effect of CYP1A2 and 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 of a strong CYP1A2 or CYP2B6 inducer with fenfluramine 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.

Coadministration of a single 0.35 mg/kg dose of fenfluramine with fluvoxamine (a strong CYP1A2 inhibitor) at steady state (50 mg once daily) in healthy volunteers increased the AUC0-t of fenfluramine by a ratio of 2.1-fold and the Cmax by a ratio of 1.2-fold, and decreased the AUC0-t of norfenfluramine by a ratio of 1.3-fold and the Cmax by a ratio of 1.4-fold, as compared to fenfluramine administered alone.

Coadministration of a single 0.35 mg/kg dose of fenfluramine with paroxetine (a strong CYP2D6 inhibitor) at steady state (30 mg once daily) in healthy volunteers increased the AUC0-t of fenfluramine by a ratio of 1.8-fold and the Cmax by a ratio of 1.1-fold, and decreased the AUC0-t of norfenfluramine by a ratio of 1.2-fold and the Cmax by a ratio of 1.3-fold, as compared to fenfluramine administered alone.

Excipients
This medicinal product contains sodium ethyl para-hydroxybenzoate (E 215) and sodium methyl para hydroxybenzoate (E 219) which 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 medicinal product. This medicinal product contains less than 1 mmol sodium (23 mg) per the maximum daily dose of 12 mL, that is to say essentially 'sodium-free'. This medicinal product contains glucose which may be harmful to the teeth.

For further safety information and full prescribing information visit: Fintepla, INN-fenfluramine (europa.eu)

About FINTEPLA® (fenfluramine) oral solution in the U.S.[9]

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.

In the United States, FINTEPLA is available only through a restricted distribution program called the FINTEPLA REMS program. Further information is available at www.FinteplaREMS.com or by telephone at +1 877 964 3649.

Important Safety Information about FINTEPLA in the U.S.[9]

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.**
- **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: 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 mm Hg).

FINTEPLA REMS Program: 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 valvular heart disease and pulmonary arterial hypertension, the need for baseline (pretreatment) and periodic cardiac monitoring via echocardiogram during treatment, and cardiac monitoring after treatment. Patients must enroll in the FINTEPLA REMS and comply with ongoing monitoring requirements. The pharmacy must be certified by enrolling in

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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. Weight should be monitored regularly, and dose modifications should be considered if weight decreases.

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. Patients treated with an AED 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 must balance the risk of suicidal thoughts or behaviors with the risks of untreated illness. Epilepsy is associated with morbidity and mortality and an increased risk of suicidal thoughts and behaviors.

Withdrawal of Antiepileptic Drugs: FINTEPLA should 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.

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, have 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 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 were diarrhea; decreased appetite; fatigue; somnolence; vomiting.

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, for additional Important Safety Information on FINTEPLA.

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UCB News

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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.

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References:

1. Clinical Trials.gov. 'A Study to Test Efficacy and Safety of Rozanolixizumab in Adult Patients With Generalized Myasthenia Gravis'. https://clinicaltrials.gov/ct2/show/NCT03971422. (Accessed March 2023).
2. Clinical Trials.gov. 'Safety, Tolerability, and Efficacy of Zilucoplan in Subjects With Generalized Myasthenia Gravis (RAISE)' https://clinicaltrials.gov/ct2/show/NCT04115293. (Accessed March 2023).
3. Smith B, et al. Generation and characterization of a high affinity anti-human FcRn antibody, rozanolixizumab, and the effects of different molecular formats on the reduction of plasma IgG concentration. MAbs. 2018;10:1111-30.
4. Kiessling P, et al. The FcRn inhibitor rozanolixizumab reduces human serum IgG concentration: A randomized phase 1 study. Sci Transl Med. 2017;9(414:eaan1208).
5. Howard J, et al. Clinical Effects of the Self-administered Subcutaneous Complement Inhibitor Zilucoplan in Patients With Moderate to Severe Generalized Myasthenia Gravis: Results of a Phase 2 Randomized, Double-Blind, Placebo-Controlled, Multicenter Clinical Trial. JAMA Neurol 2022 1;77(5):582-592.
6. BRIVIACT® EU SmPC. https://www.ema.europa.eu/en/documents/product-information/briviact-epar-product-information_en.pdf (Accessed March 2023).
7. BRIVIACT® (brivaracetam): U.S. prescribing information. Smyrna, GA: UCB, Inc. https://ucb-usa.com/sites/default/files/2022-08/Briv%20prescribing%202022.pdf?_gl=1*1hzddm7*_ga*MTYwMzA2MTA3Mi4xNjc1MjQ5ODgx*_ga_TXC8S80N6W*MTY4MTg4ODgzNC4xMy4xLjE2ODE4ODg5MTMuNTAuMC4w (Accessed March 2023)
8. FINTEPLA® EU SmPC.https://www.ema.europa.eu/en/documents/product-information/fintepla-epar-product-information_en.pdf. (Accessed March 2023)
9. FINTEPLA® (fenfluramine): U.S. prescribing information. Smyrna, GA: UCB, Inc. https://www.ucb-usa.com/sites/default/files/2023-03/Fintepla_Current_COL_Rev_03-2023_17_March_2023.pdf (Accessed March 2023)