

## Fintepla▼ (fenfluramine) Prescribing information

Please refer to the full Summary of Product Characteristics (SmPC) before prescribing. **Indications:** Treatment of seizures associated with Dravet syndrome as an add-on therapy to other anti-epileptic medicines for patients 2 years of age and older. **Presentation:** 2.2 mg/mL oral solution. Each mL contains 2.2mg of fenfluramine (as fenfluramine hydrochloride).

**Dosage and Administration:** Please refer to SmPC for full information/dosing tables. *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). **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. **Special populations:** *Renal impairment:* No clinical data available. *Hepatic impairment:* No clinical data available. Not recommended in moderate or severe liver impairment. *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. If echocardiogram findings suggestive of pulmonary arterial hypertension, perform a repeat echocardiogram as soon as possible and within 3 months to confirm these findings. If echocardiogram finding is confirmed suggestive of an increased probability of pulmonary arterial hypertension defined as intermediate probability, conduct a benefit-risk evaluation of continuation of Fintepla by the prescriber, carer and cardiologist. If echocardiogram suggests a high probability, it is recommended fenfluramine treatment should be stopped. *Decreased appetite and weight loss:* Fenfluramine can cause decreased appetite and weight loss - an additive effect can occur in combination with other anti-epileptic medicines such as stiripentol. Monitor the patient's weight. Undertake risk-benefit evaluation before starting treatment if history of anorexia nervosa or bulimia nervosa. *Fintepla controlled access programme.* A controlled access programme has been created to 1) prevent off-label use in weight management in obese patients and 2) confirm that prescribing physicians have been informed of the need for periodic cardiac monitoring in patients taking Fintepla. *Somnolence:* Fenfluramine can cause somnolence which could be potentiated by other central nervous system depressants. *Suicidal behaviour and ideation.* Suicidal behaviour and ideation have been reported in patients treated with anti-epileptic medicines in several indications. Advise patients and caregivers to seek medical advice should any signs of suicidal behaviour and ideation emerge. *Serotonin syndrome:* Serotonin syndrome, a potentially life-threatening condition, may occur with fenfluramine treatment, particularly with concomitant use of other serotonergic agents; with agents that impair metabolism of serotonin such as MAOIs; or with antipsychotics that may affect the serotonergic neurotransmitter systems. Carefully observe the patient, particularly during treatment initiation and dose increases. *Increased seizure frequency:* A clinically relevant increase in

seizure frequency may occur during treatment, which may require adjustment in the dose of fenfluramine and/or concomitant anti-epileptic medicines, or discontinuation of fenfluramine, should the benefit-risk be negative. *Cyproheptadine:* Cyproheptadine is a potent serotonin receptor antagonist and may therefore decrease the efficacy of fenfluramine. If cyproheptadine is added to treatment with fenfluramine, monitor patient for worsening of seizures. If fenfluramine treatment is initiated in a patient taking cyproheptadine, fenfluramine's efficacy may be reduced. *Glaucoma.* Fenfluramine can cause mydriasis and can precipitate angle closure glaucoma. Discontinue therapy in patients with acute decreases in visual acuity. Consider discontinuation if ocular pain of unknown origin. *Strong CYP1A2 or CYP2B6 inducers.* Co-administration with strong CYP1A2 inducers or CYP2B6 inducers may decrease fenfluramine plasma concentrations. Consider an increase in fenfluramine dosage when co-administered with a strong CYP1A2 or CYP2B6 inducer; do not exceed the maximum daily dose. *Excipients.* Contains sodium ethyl parahydroxybenzoate (E 215) and sodium methyl parahydroxybenzoate (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.

**Drug interaction:** Pharmacodynamic interactions with other CNS depressants increase the risk of aggravated central nervous system depression. Examples of such depressants are other serotonergic agents (including SSRIs, SNRIs, tricyclic antidepressants, or triptans); agents that impair metabolism of serotonin such as MAOIs; or antipsychotics that may affect the serotonergic neurotransmitter systems. 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:** *Pregnancy:* Limited data in pregnant women. As a precaution, avoid use of Fintepla in pregnancy. *Breast-feeding:* 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. **Ability to 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. **Undesirable effects:** *Very common (≥1/10):* Bronchitis, upper respiratory tract infection, decreased appetite, lethargy, somnolence, status epilepticus, tremor, constipation, diarrhoea, vomiting, pyrexia, fatigue, blood glucose decreased, echocardiogram abnormal (trace regurgitation), weight decreased and fall. *Common (≥1/100 to <1/10):* Ear infection, abnormal behaviour and irritability. Refer to SmPC for other adverse reactions. **Overdose:** Limited data concerning clinical effects and management of overdose. Agitation, drowsiness, confusion, flushing, tremor (or shivering), fever, sweating, abdominal pain, hyperventilation, and dilated non-reactive pupils were reported at much higher doses of fenfluramine than those included in the clinical trial program. Treatment should include gastric lavage. Monitor vital functions closely, and administer supportive treatment in case of convulsions, arrhythmias, or respiratory difficulties. **Package quantities and Marketing Authorisation number:** Fintepla is presented in a white bottle with oral syringes included which should be used to administer the prescribed dose. Bottle sizes of 60 mL, 120 mL and 360 mL. EU/1/20/1491/001, EU/1/20/1491/002 and EU/1/20/1491/004. **Legal Category:** POM. **Marketing Authorisation Holder:** Zogenix ROI Ltd, Trinity House, Charleston Road, Ranelagh, Dublin 6 D06 C8X4 Ireland. **Job Code:** EU-FIN1-2000087 **Date of Preparation:** December 2020

Adverse events should be reported.  
Please refer to section 4.8 of the SmPC for national reporting requirements in your country. Adverse events should also be reported to Zogenix International Limited on 0800 060 8767 or email [medinfo.eu@zogenix.com](mailto:medinfo.eu@zogenix.com)

## Fintepla▼ (fenfluramine) Prescribing information

Please refer to the full Summary of Product Characteristics (SmPC) before prescribing. **Indications:** Treatment of seizures associated with Dravet syndrome as an add-on therapy to other anti-epileptic medicines for patients 2 years of age and older. **Presentation:** 2.2 mg/mL oral solution. Each mL contains 2.2mg of fenfluramine (as fenfluramine hydrochloride).

**Dosage and Administration:** Please refer to SmPC for full information.

**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). **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. **Special populations: Renal impairment:** No clinical data available. **Hepatic impairment:** No clinical data available. Not recommended in moderate or severe liver impairment. **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. If echocardiogram findings suggestive of pulmonary arterial hypertension, perform a repeat echocardiogram as soon as possible and within 3 months to confirm these findings. If echocardiogram finding is confirmed suggestive of an increased probability of pulmonary arterial hypertension defined as intermediate probability, conduct a benefit-risk evaluation of continuation of Fintepla by the prescriber, carer and cardiologist. If echocardiogram suggests a high probability, it is recommended fenfluramine treatment should be stopped. **Decreased appetite and weight loss:** Fenfluramine can cause decreased appetite and weight loss - an additive effect can occur in combination with other anti-epileptic medicines such as stiripentol. Monitor the patient's weight. Undertake risk-benefit evaluation before starting treatment if history of anorexia nervosa or bulimia nervosa. **Fintepla controlled access programme.** A controlled access programme has been created to 1) prevent off-label use in weight management in obese patients and 2) confirm that prescribing physicians have been informed of the need for periodic cardiac monitoring in patients taking Fintepla. **Somnolence:** Fenfluramine can cause somnolence which could be potentiated by other central nervous system depressants. **Suicidal behaviour and ideation.** Suicidal behaviour and ideation have been reported in patients treated with anti-epileptic medicines in several indications. Advise patients and caregivers to seek medical advice should any signs of suicidal behaviour and ideation emerge. **Serotonin syndrome:** Serotonin syndrome, a potentially life-threatening condition, may occur with fenfluramine treatment, particularly with concomitant use of other serotonergic agents; with agents that impair metabolism of serotonin such as MAOIs; or with antipsychotics that may affect the serotonergic neurotransmitter systems. Carefully observe the patient, particularly during treatment initiation and dose increases. **Increased seizure frequency:** A clinically relevant increase in seizure frequency may occur during treatment, which may require adjustment in the dose of fenfluramine and/or concomitant anti-epileptic medicines, or

discontinuation of fenfluramine, should the benefit-risk be negative. **Cyproheptadine:** Cyproheptadine is a potent serotonin receptor antagonist and may therefore decrease the efficacy of fenfluramine. If cyproheptadine is added to treatment with fenfluramine, monitor patient for worsening of seizures. If fenfluramine treatment is initiated in a patient taking cyproheptadine, fenfluramine's efficacy may be reduced. **Glaucoma.** Fenfluramine can cause mydriasis and can precipitate angle closure glaucoma. Discontinue therapy in patients with acute decreases in visual acuity. Consider discontinuation if ocular pain of unknown origin. **Strong CYP1A2 or CYP2B6 inducers.** Co-administration with strong CYP1A2 inducers or CYP2B6 inducers may decrease fenfluramine plasma concentrations. Consider an increase in fenfluramine dosage when co-administered with a strong CYP1A2 or CYP2B6 inducer; do not exceed the maximum daily dose. **Excipients.** Contains sodium ethyl parahydroxybenzoate (E 215) and sodium methyl parahydroxybenzoate (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.

**Drug interaction:** Pharmacodynamic interactions with other CNS depressants increase the risk of aggravated central nervous system depression. Examples of such depressants are other serotonergic agents (including SSRIs, SNRIs, tricyclic antidepressants, or triptans); agents that impair metabolism of serotonin such as MAOIs; or antipsychotics that may affect the serotonergic neurotransmitter systems. 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:**

**Pregnancy:** Limited data in pregnant women. As a precaution, avoid use of Fintepla in pregnancy. **Breast-feeding:** 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. **Ability to 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. **Undesirable effects: Very common (≥1/10):** Bronchitis, upper respiratory tract infection, decreased appetite, lethargy, somnolence, status epilepticus, tremor, constipation, diarrhoea, vomiting, pyrexia, fatigue, blood glucose decreased, echocardiogram abnormal (trace regurgitation), weight decreased and fall. **Common (≥1/100 to <1/10):** Ear infection, abnormal behaviour and irritability. Refer to SmPC for other adverse reactions. **Overdose:** Limited data concerning clinical effects and management of overdose. Agitation, drowsiness, confusion, flushing, tremor (or shivering), fever, sweating, abdominal pain, hyperventilation, and dilated non-reactive pupils were reported at much higher doses of fenfluramine than those included in the clinical trial program. Treatment should include gastric lavage. Monitor vital functions closely, and administer supportive treatment in case of convulsions, arrhythmias, or respiratory difficulties. **Package quantities and Marketing Authorisation number:** Fintepla is presented in a white bottle with oral syringes included which should be used to administer the prescribed dose. Bottle sizes of 60 mL, 120 mL and 360 mL. EU/1/20/1491/001, EU/1/20/1491/002 and EU/1/20/1491/004. **Legal Category:** POM. **Marketing Authorisation Holder:** Zogenix ROI Ltd, Trinity House, Charleston Road, Ranelagh, Dublin 6 D06 C8X4 Ireland. **Maximum NHS List Price:** Bottle sizes of 60mL = £901.44, 120mL = £1802.88 and 360mL = £5408.65

**Job Code:** UK- FIN1-2100051 **Date of Preparation:** August 2021

**Adverse events should be reported.**  
Reporting forms and information can be found at <https://yellowcard.mhra.gov.uk/> or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Zogenix International Limited on 0800 060 8767 or email [medinfo.eu@zogenix.com](mailto:medinfo.eu@zogenix.com).

**Adverse events should be reported.**  
Reporting forms and information can be found at <https://yellowcard.mhra.gov.uk/> or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Zogenix International Limited on 0800 060 8767 or email [medinfo.eu@zogenix.com](mailto:medinfo.eu@zogenix.com).