Dosing and Titration Information

Fintepla®
(fenfluramine) CIV
2.2 mg/mL oral solution

FINTEPLA is approved for the treatment of seizures associated with Dravet syndrome and Lennox-Gastaut syndrome in patients 2 years of age and older.

Flexible dosing to meet the needs of your patients

- FINTEPLA is a cherry-flavored, oral solution that may be administered with or without food
- The starting dose is 0.1 mg/kg twice daily, and the maximum dose is 0.35 mg/kg twice daily
- Administration of FINTEPLA to patients with hepatic impairment is not recommended

Recommended weight-based dosing (without stiripentol)*

Dravet Syndrome	
Initial Dose	0.1 mg/kg twice daily
Titration Dose (Day 7)	0.2 mg/kg twice daily
Maximum Dose (Day 14)	0.35 mg/kg twice daily
MAXIMUM TOTAL DAILY DOSE	**26 mg**

LGS	
Initial Dose	0.1 mg/kg twice daily
Titration Dose (Day 7)	0.2 mg/kg twice daily
Maintenance Dose (Day 14)	0.35 mg/kg twice daily
MAXIMUM TOTAL DAILY DOSE	**26 mg**

*For patients not on concomitant stiripentol in whom a more rapid titration is warranted, the dose may be increased every 4 days.

For patients taking FINTEPLA who are being treated with strong CYP1A2 or CYP2D6 inhibitors or who have severe renal impairment, and are not on concomitant stiripentol, the maximum daily dose is **20 mg**.

For patients taking FINTEPLA with concomitant stiripentol plus clobazam, the initial dose is 0.1 mg/kg twice daily, the day 7 dose is 0.15 mg/kg twice daily, and the day 14 dose is 0.2 mg/kg twice daily. The maximum daily dose is **17 mg**.

FINTEPLA is the next step in your patients' current antiseizure treatment regimens

- No dose adjustments to current antiseizure medications (ASMs) are required when adding FINTEPLA to patients' already complex treatment regimens (including cannabidiol, clobazam, valproate, stiripentol, and a ketogenic diet)
- FINTEPLA has not shown a clinically significant impact on the pharmacokinetics of other ASMs
- When discontinuing FINTEPLA, the dose should be decreased gradually. Abrupt discontinuation should be avoided when possible to minimize the risk of increased seizure frequency and status epilepticus

Calculating the dose

Example for a patient who weighs 70 lb:

70 lb ÷ 2.2 lb/kg = 32 kg

32 kg × 0.1 mg/kg (starting dose) =
3.2 mg twice daily

3.2 mg ÷ 2.2 mg/mL FINTEPLA =
1.5 mL twice daily

Prescription example

FINTEPLA (fenfluramine 2.2 mg/mL)

Sig: Take 5 mL PO BID (titrate as described below)

Week 1, take 1.5 mL PO BID
Week 2, take 3 mL PO BID
Week 3 and ongoing, take 5 mL PO BID

Weight: 32 kg
Diagnosis: Seizures associated with Dravet syndrome

Days' supply 30 Refill 5 times Dispense as written ☑

Where to get FINTEPLA

- FINTEPLA is dispensed exclusively by the Zogenix Central pharmacy partner, AnovoRx. If you have questions about a patient's prescription or about refills, contact AnovoRx at 1-844-288-5007 (8:00 AM to 5:00 PM Central Time, Monday through Friday) or send a fax to 1-855-813-2039

Please visit FinteplaHCP.com/dosing-schedule for an interactive FINTEPLA dosing calculator.

INDICATIONS AND USAGE

FINTEPLA® (fenfluramine) oral solution, CIV, 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.

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

Please see Important Safety Information on next page and accompanying full Prescribing Information, including Boxed Warning.

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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 >35mmHg).

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 valvular heart disease and pulmonary arterial hypertension, how to recognize signs and symptoms of valvular heart disease and pulmonary arterial hypertension, 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.

Warnings and Precautions (cont.)

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.

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

Administration to patients with hepatic impairment is not recommended.

To report SUSPECTED ADVERSE REACTIONS, contact Zogenix Inc. at 1-866-964-3649 (1-866-Zogenix) 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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