Fintepla® (fenfluramine) – New orphan drug approval

- On June 25, 2020, the FDA announced the approval of Zogenix's Fintepla (fenfluramine), for the treatment of seizures associated with Dravet syndrome in patients 2 years of age and older.
    - Fintepla is a Schedule IV controlled substance.
- Dravet syndrome is a rare childhood-onset epilepsy marked by frequent debilitating seizures, lifelong developmental and motor impairments, and an increased risk of sudden death.
- The mechanisms by which Fintepla exerts its therapeutic effects in the treatment of seizures associated with Dravet syndrome are unknown.
- The efficacy of Fintepla was established in two randomized, double-blind, placebo-controlled studies in patients 2 to 18 years of age with Dravet syndrome. Study 1 (N = 117) compared a 0.7 mg/kg/day and a 0.2 mg/kg/day dose of Fintepla with placebo in patients who were not receiving stiripentol (Diacomit®). Study 2 (N = 85) compared a 0.4 mg/kg/day dose of Fintepla with placebo in patients who were receiving stiripentol and either clobazam, valproate, or both. The primary efficacy endpoint in both studies was the change from baseline in the frequency of convulsive seizures per 28 days during the combined 14-week (study 1) or 15-week (study 2) titration and maintenance periods.
    - In study 1 and study 2, the reduction in convulsive seizure frequency per 28 days was statistically significantly greater for all dose groups of Fintepla vs. placebo.

Convulsive seizure frequency (per 28 days)	Placebo	Fintepla 0.2 mg/kg/day	Fintepla 0.7 mg/kg/day	Fintepla 0.4 mg/kg/day
Study 1	**N = 39**	**N = 38**	**N = 40**	--
Baseline period median	29.4	18.1	18.7	--
% difference vs. placebo	--	-31.7%	-70.0%	--
p-value vs. placebo	--	0.043	< 0.001	--
Study 2	**N = 42**	**N/A**	**N/A**	**N = 43**
Baseline period median	11.5	--	--	15.0
% difference vs. placebo	--	--	--	-59.5%
p-value vs. placebo	--	--	--	< 0.001

- Fintepla carries a boxed warning for valvular heart disease and pulmonary arterial hypertension.
    - Due to the risks of valvular heart disease and pulmonary arterial hypertension, Fintepla is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Fintepla REMS.
- Fintepla is contraindicated in patients with:
    - Hypersensitivity to fenfluramine or any of the excipients in Fintepla
    - Concomitant use of, or within 14 days of the administration of monoamine oxidase inhibitors because of an increased risk of serotonin syndrome.

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- Additional warnings and precautions for Fintepla include decreased appetite and decreased weight; somnolence, sedation, and lethargy; suicidal behavior and ideation; withdrawal of antiepileptic drugs; serotonin syndrome; increase in blood pressure; and glaucoma.

- The most common adverse reactions (≥ 10% and > placebo) with Fintepla use were decreased appetite; somnolence, sedation, lethargy; diarrhea; constipation; abnormal echocardiogram; fatigue, malaise, asthenia; ataxia, balance disorder, gait disturbance; increased blood pressure; drooling, salivary hypersecretion; pyrexia; upper respiratory tract infection; vomiting; decreased weight; fall; and status epilepticus.

- The initial starting and maintenance dosage of Fintepla is 0.1 mg/kg orally twice daily, which can be increased weekly based on efficacy and tolerability. Refer to the drug label for the recommended titration schedule.

    — Patients not on concomitant stiripentol who are tolerating Fintepla at 0.1 mg/kg twice daily and require further reduction of seizures may benefit from a dosage increase up to a maximum recommended maintenance dosage of 0.35 mg/kg twice daily (maximum daily dosage of 26 mg).
    — Patients taking concomitant stiripentol and clobazam who are tolerating Fintepla at 0.1 mg/kg twice daily and require further reduction of seizures may benefit from a dosage increase up to a maximum recommended maintenance dosage of 0.2 mg/kg twice daily (maximum daily dosage of 17 mg).

- Zogenix plans to launch Fintepla in July. Fintepla will be available as a 2.2 mg/mL oral solution.