Fintepla (fenfluramine) Prior Authorization with Quantity Limit Program Summary

POLICY REVIEW CYCLE

Effective Date **Date of Origin**
3/1/2023

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Fintepla® (fenfluramine) Oral solution	Treatment of seizures associated with Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS) in patients 2 years of age and older		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Dravet Syndrome	Dravet syndrome (DS) is a severe form of epilepsy characterized by frequent, prolonged seizures and neurodevelopmental problems beginning in infancy. Mutations in the alpha-1 subunit of the voltage-gated sodium channel (*SCN1A*) gene are identified in 70-85% of patients with DS. Status epilepticus, or a seizure lasting longer than 5 minutes and sometimes 30 minutes or more, is common. Additional seizure types, including myoclonic, atypical absence, and complex partial seizures, appear before age 5 years. Mortality in DS is elevated above that found in the general epilepsy population, with an estimated mortality of 15-20% by adulthood. First-line treatment is typically valproate, with clobazam added if needed. Additional agents include stiripentol, topiramate, and levetiracetam. For patients with symptoms refractory to drug therapy, ketogenic diet and vagal nerve stimulation may be beneficial.(2-4) The mechanisms by which fenfluramine exerts its therapeutic effects in the treatment of seizures associated with DS are unknown. Fenfluramine and its metabolite, norfenfluramine, increase extracellular levels of serotonin through interaction with serotonin transporter proteins, and exhibit agonist activity at serotonin 5HT-2 receptors.(1)
Lennox-Gastaut Syndrome	Lennox-Gastaut syndrome (LGS) is a severe form of epilepsy that typically becomes apparent during infancy or early childhood. The syndrome has many causes, including genetic disorders, cortical malformations, tumors, encephalopathies following hypoxic-ischemic insults, meningitis, and head injuries. Affected children experience several different types of seizures; atonic, clonic, and atypical absence seizures are the most common. Children with LGS may develop cognitive dysfunction, delays in reaching developmental milestones, and behavioral problems. LGS is difficult to treat because no specific therapy is effective in all cases, and the disorder has proven particularly resistant to most therapeutic options. Valproate is generally considered first-line therapy, and if monotherapy is ineffective another drug such as lamotrigine, topiramate, rufinamide, or clobazam may be added as adjunctive therapy. Additional therapies combined with drug therapy, for patients who do not respond, include the ketogenic diet and vagal nerve stimulation.(7)

Efficacy	The effectiveness of fenfluramine for the treatment of seizures associated with Dravet syndrome in patients 2 years of age and older was established in two randomized, double-blind, placebo-controlled trials in patients 2 to 18 years of age. Study 1 (N = 117) compared a 0.7 mg/kg/day and a 0.2 mg/kg/day dose of fenfluramine with placebo in patients who were NOT receiving stiripentol. Study 2 (N = 85) compared a 0.4 mg/kg/day dose of fenfluramine with placebo in patients who were receiving stiripentol and either clobazam, valproate, or both. In both studies, patients had a clinical diagnosis of Dravet syndrome and were inadequately controlled on at least one antiepileptic drug (AED) or other antiseizure treatment including vagal nerve stimulation or a ketogenic diet. In Study 1, 98% of patients were taking 1-4 concomitant AEDs; in Study 2, 100% were taking 2-4 concomitant AEDs.(1,5,6) The primary efficacy endpoint in both studies was the change from baseline in the frequency of convulsive seizures per 28 days during the treatment period. For Study 1, the percent reduction in monthly convulsive seizure frequency was 70% for the 0.7 mg/kg/day dose (P less than 0.001) and 31.7% for the 0.2 mg/kg/day dose (P = 0.043); for Study 2 it was 59.5% reduction (P less than 0.001). A reduction in convulsive seizures was observed within 3-4 weeks of starting fenfluramine, and the effect remained generally consistent over the 14- or 15-week treatment period.(1,5,6) A secondary endpoint was longest seizure-free interval, for which the median longest seizure-free intervals in the 0.7 mg/kg/day, 0.4 mg/kg/day, and 0.2 mg/kg/day groups were 25 days, 22 days, and 15 days, respectively.(5,6) The effectiveness of fenfluramine for the treatment of seizures associated with LGS in patients 2 years of age and older was established in a randomized, double-blind, placebo-controlled trial in patients 2 to 35 years of age. Study 3 (N=263) compared a 0.7 mg/kg/day and a 0.2 mg/kg/day dose of fenfluramine with placebo in patients with a diagnosis of LGS who were inadequately controlled on at least one antiepileptic drug (AED) or other antiseizure treatment including vagal nerve stimulation and/or a ketogenic diet.(1) The primary efficacy endpoint was the median percent change from baseline (reduction) in the frequency of seizures per 28 days during the treatment period. The median percent change from baseline (reduction) in the frequency of seizures per 28 days was significantly greater for the 0.7 mg/kg/day group compared with placebo (80%; p=0.0037). The effect remained generally consistent over the 14-week treatment period.(1)
Safety	Fintepla carries a boxed warning for valvular heart disease and pulmonary arterial hypertension. There is an association between serotonergic drugs with 5-HT2B receptor agonist activity, including fenfluramine, and valvular heart disease and pulmonary arterial hypertension. Echocardiogram assessments are required before, during, and after treatment with Fintepla; benefits versus risks of initiating or continuing must be considered based on echocardiogram findings. Because of these risks, Fintepla is available only through the Fintepla REMS program.(1) Fintepla has the following contraindications:(1) • Concomitant use of, or within 14 days of the administration of, monoamine oxidase inhibitors because of an increased risk of serotonin syndrome. • Hypersensitivity to fenfluramine or any of the excipients in Fintepla.

REFERENCES

Number	Reference
1	Fintepla prescribing information. Zogenix, Inc. March 2022.

Number	Reference
2	Wirrell EC, Laux L, Donner E, et al. Optimizing the Diagnosis and Management of Dravet Syndrome: Recommendations from a North American Consensus Panel. Pediatr Neurol. 2017;68:18-34.
3	Sullivan J, Knupp K, Wirrell E. Dravet Syndrome. National Organization for Rare Disorders (NORD). Available at https://rarediseases.org/rare-diseases/dravet-syndrome-spectrum/.
4	Andrade DM, Nascimento FA, et al. Dravet Syndrome: Management and Prognosis. UpToDate. Literature review current through November 2021. Last updated November 2021.
5	Lagae L, Sullivan J, Knupp K, et al. Fenfluramine Hydrochloride for the Treatment of Seizures in Dravet Syndrome: A Randomized, Double-Blind, Placebo-Controlled Trial. Lancet. 2019;394(10216):2243-2254.
6	Nabbout R, Mistry A, Zuberi S, et al. Fenfluramine for Treatment-Resistant Seizures in Patients with Dravet Syndrome Receiving Stiripentol-Inclusive Regimens: A Randomized Clinical Trial. JAMA Neurol. 2020;77(3):300-308.
7	Wheeless JW. Lennox-Gastaut Syndrome. National Organization for Rare DIsorders (NORD). Last updated 2020. Available at https://rarediseases.org/rare-diseases/lennox-gastaut-syndrome/.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Preferred Status	Effective Date
Fintepla	fenfluramine hcl oral soln	2.2 MG/ML	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Days Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist	Effective Date
Fintepla	Fenfluramine HCl Oral Soln 2.2 MG/ML	2.2 MG/ML	360.0	MLS	30	Days				

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Fintepla	fenfluramine hcl oral soln	2.2 MG/ML	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Fintepla	Fenfluramine HCl Oral Soln 2.2 MG/ML	2.2 MG/ML	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. BOTH of the following: 1. The patient has a diagnosis of seizure associated with Dravet syndrome (DS) or Lennox-Gastaut syndrome (LGS) **AND** 2. The requested agent will NOT be used as monotherapy for seizure management **OR** B. The patient has another FDA approved indication for the requested agent and route of administration **AND** 2. ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 3. An echocardiogram assessment will be obtained before and during treatment with the requested agent, to evaluate for valvular heart disease and pulmonary arterial hypertension **AND** 4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent

Module	Clinical Criteria for Approval
	Length of Approval: 12 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria section below. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. If using for seizure management, the requested agent will NOT be used as monotherapy **AND** 4. An echocardiogram assessment will be obtained during treatment with the requested agent, to evaluate for valvular heart disease and pulmonary arterial hypertension **AND** 5. The prescriber is a specialist in the area of the patient's diagnosis (e.g., neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 6. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria section below.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity Limits for the Target Agent(s) will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **Length of Approval:** 12 months