Clinical Policy: Fenfluramine (Fintepla)

Reference Number: CP.PMN.246
Effective Date: 09.01.20
Last Review Date: 08.22
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Fenfluramine (Fintepla®) is a serotonin transporter protein modulator and exhibits agonist activity at serotonin 5HT-2 receptors.

FDA Approved Indication(s)

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.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Fintepla is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Dravet Syndrome or Lennox-Gastaut Syndrome (must meet all)**:**

1. Diagnosis of DS or LGS;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 2 years;
4. Will be used as adjunctive therapy (*see Appendix B*) with at least one other antiepileptic drug;
5. For LGS, failure of two of the following, unless clinically significant adverse effects are experienced or all are contraindicated: clobazam, clonazepam, felbamate, lamotrigine, rufinamide, topiramate;
6. Failure of ≥ 3 month trial of Epidiolex® at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed either of the following (a or b):
   a. Members not on concomitant Diacomit®: 26 mg (12 mL) per day;
   b. Members on concomitant Diacomit plus clobazam: 17 mg (8 mL) per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is

NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Dravet Syndrome or Lennox-Gastaut Syndrome (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Fintepla for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Fintepla will continue to be used as adjunctive therapy (*see Appendix B*) with at least one other antiepileptic drug;
4. If request is for a dose increase, new dose does not exceed either of the following (a or b):
   a. Members not on concomitant Diacomit: 26 mg (12 mL) per day;
   b. Members on concomitant Diacomit plus clobazam: 17 mg (8 mL) per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
DS: Dravet syndrome
FDA: Food and Drug Administration
LGS: Lennox-Gastaut syndrome

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Epidiolex® (cannabidiol)	Initial: 2.5 mg/kg PO BID Maintenance: 5 mg/kg PO BID	20 mg/kg/day
topiramate (Topamax®, Qudexy® XR)	**LGS** • Adults and Adolescents 17 years and older: Initial dose is 25 to 50 mg/day orally. Maintenance dose is 200 to 400 mg/day orally (divided and given twice daily). • Children and Adolescents 2 to 16 years: Initial dose is 1 to 3 mg/kg/day (max: 25 mg/day) orally once daily in the evening. Maintenance dose is 5 to 9 mg/kg/day orally. **DS**‡ Initial dose is 0.5 to 2 mg/kg/day orally. Max target dose is 8 to 12 mg/kg/day orally.	LGS: Age ≥ 17: 400 mg/day Age 2 – 16: 25 mg/day DS: 8 to 12 mg/kg/day
lamotrigine (Lamictal® CD, ODT, XR, & Subvenite®)	**LGS**‡ • Patients receiving enzyme-inducing AEDs (e.g., carbamazepine, phenobarbital, phenytoin, primidone) NOT to include valproate: o Adults and Adolescents: Initial dose is 50 mg orally daily. Maintenance dose is 300 to 500 mg/day orally given in 2 divided doses. o Children 2 to 12 years: Initial dose is 0.6 mg/kg/day orally in 2 divided doses. Maintenance dose is 5 to 15 mg/kg/day (max 400 mg/day) orally given in 2 divided doses. • Patients receiving valproate: o Adults and Adolescents: Initial dose is 25 mg orally every other day is given for 2 weeks. Maintenance dose is 100 to 400 mg/day orally, given in 1 to 2 divided doses. o Children 2 to 12 years: Dosage depends on weight. **DS**‡ Avoid lamotrigine and other sodium channel agents since they can exacerbate seizures associated with Dravet Syndrome.	With valproate: 100 mg/day With enzyme-inducing drugs: 400 mg/day
felbamate (Felbatol®)	**LGS** Adolescents and Children 2 - 14 years: Add felbamate at 15 mg/kg/day orally in 3-4 divided doses while reducing doses of other AEDs by 20-30%. Increase felbamate dose by 15 mg/kg/day increments at weekly intervals to 45 mg/kg/day orally. Max dose is 3,600 mg/day orally.	3,600 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
rufinamide (Banzel®)	**LGS** • Adults and Adolescents ≥ 17 years: Initial dose is 400-800 mg/day orally in 2 equally divided doses. Target and max dose is 3,200 mg/day orally given in 2 equally divided doses. • Children and Adolescents 1-16 years: Initial dose is 10 mg/kg/day orally given as 2 equally divided doses. Maintenance target dose is 45 mg/kg/day or 3,200 mg/day orally, whichever is less, given in 2 equally divided doses. **DS** Avoid rufinamide and other sodium channel agents since they can exacerbate seizures associated with Dravet Syndrome.	3,200 mg/kg/day
clobazam (Onfi®)	**LGS** For Adults, Adolescents, & Children older than 2 years: • Patients weighing > 30 kg: Initial dose is 5 mg orally twice daily. Max dose is 20 mg orally twice daily. Dosing should be individualized based upon efficacy and tolerability. • Patients weighing ≤ 30 kg: Initial dose is 5 mg orally once daily. Max dose is 10 mg orally twice daily. Dosing should be individualized based upon efficacy and tolerability. **DS**‡ Initial dose is 0.2 to 0.3 mg/kg/day PO. Max target dose is 0.5 to 2 mg/kg/day PO.	LGS: ≤ 30 kg: 0.2 mg/kg/day > 30 kg: 20 mg/day DS: 2 mg/kg/day
clonazepam (Klonopin®)	**LGS** For Adults, Adolescents, & Children: • Patients weighing > 30 kg: Initial dose is 1.5 mg/day orally, given in three equally divided doses. Max dose is 20 mg/day orally, given in three equally divided doses. Patients weighing ≤ 30 kg: Initial dose is 0.01 to 0.03 mg/kg/day orally, given in three equally divided doses. Max dose is 0.1 to 0.2 mg/kg/day orally, given in three equally divided doses.	≤ 30 kg: 0.2 mg/kg/day > 30 kg: 20 mg/day
valproic acid (Depakene®, Depakote®, Stavzor®)	**LGS**‡ Initial dose is 7 to 10 mg/kg/day PO, given three to four times daily for non enteric-coated capsules or syrup, BID for delayed-release tablets, and QD for the extended release preparation. A typical adult	LGS: 60 mg/kg/day or 3,000 mg/day DS: 60 mg/kg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	starting dose is 500 mg QD. The max dose is 60 mg/kg/day or 3,000 mg/day. **DS**‡ Initial dose is 10 to 15 mg/kg/day PO, given in two to three equally divided doses. Max target dose is 25 to 60 mg/kg/day PO, given in two to three equally divided doses, depending on achieved blood levels.	
levetiracetam (Spritam®, Keppra®)	**LGS**‡ Initial dose is 5 mg/kg/day PO, given in two or three equal doses per day. Max dose is 20 to 80 mg/kg/day PO, according to effectiveness and tolerability. **DS**‡ Initial dose is 10 to 20 mg/kg/day PO, divided twice daily or three times daily. Max dose is 60 to 80 mg/kg/day PO, divided twice daily or three times daily.	80 mg/kg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hypersensitivity to fenfluramine or any of the excipients in Fintepla, concomitant use, or within 14 days of the administration of, monoamine oxidase inhibitors because of an increased risk of serotonin syndrome
- Boxed warning(s): valvular heart disease, pulmonary arterial hypertension

Appendix D: General Information

- Complete seizure control is typically not achievable in DS, so the primary goal of therapy is to reduce seizure frequency. The following therapies are recommended for the management of DS by a North American consensus panel (January 2017):

	North American Consensus Panel
1st line	Valproic acid or clobazam *If first choice is not effective, then add the other*
2nd line	Addition of Diacomit or topiramate
3rd line	Addition of clonazepam, levetiracetam, zonisamide, ethosuximide, or phenobarbital

- LGS is another severe form of epilepsy. Per American Academy of Neurology and the American Epilepsy Society Anti-Epileptic Pharmacologic Treatment Guidelines, the recommended treatment for drop seizures associated with LGS is lamotrigine and topiramate (Level A).

- A Cochrane Database of Systematic Review 2013 article concluded that the optimum treatment for LGS remains uncertain and no study to date has shown any one drug to be highly efficacious; rufinamide, lamotrigine, topiramate and felbamate may be helpful as add-on therapy, and clobazam may be helpful for drop seizures. Until further research has been undertaken, clinicians will need to continue to consider each patient individually, taking into account the potential benefit of each therapy weighed against the risk of adverse effects.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
DS, LGS	Initial starting and maintenance dose: 0.1 mg/kg PO BID, which can be increased weekly based on efficacy and tolerability.	No concomitant Diacomit: 26 mg/day Concomitant Diacomit and clobazam: 17 mg/day

VI. Product Availability

Oral solution: 2.2 mg/mL

VII. References

1. Fintepla Prescribing Information. Emeryville, CA: Zogenix Inc.; March 2022. Available at: www.Fintepla.com. Accessed May 12, 2022.
2. Wirrell EC, Laux L, Jette N, et al. Optimizing the diagnosis and management of Dravet syndrome: recommendations from a North American consensus panel. Pediatr Neurol. 2017; 68: 18-34.
3. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed May 12, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	07.14.20	08.20
Per November SDC and prior clinical guidance, added redirection to Epidiolex.	11.11.20	
3Q 2021 annual review: no significant changes; revised HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	04.19.21	08.21
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22
3Q 2022 annual review: no significant changes; references reviewed and updated. RT4: added criteria for newly FDA-approved indication of LGS.	05.12.22	08.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program

approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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