BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

**PHARMACY COVERAGE GUIDELINE**

# FINTEPLA® (fenfluramine) oral
# Generic Equivalent (if available)

**This Pharmacy Coverage Guideline (PCG):**
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

**Scope**
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

**Instructions & Guidance**
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

## Medical Necessity Requirements for FINTEPLA (fenfluramine)

## Criteria for Initial Therapy:

### Prescriber Qualifications
- Prescribed by a Neurologist or in consultation with a Neurologist

### Indication
- Seizures associated with Dravet syndrome on stable antiepileptic medication therapy
- Seizures associated with Lennox Gastaut syndrome on stable antiepileptic medication therapy

ORIGINAL EFFECTIVE DATE: 08/202020 | ARCHIVE DATE: | LAST REVIEW DATE: 08/21/2025 | LAST CRITERIA REVISION DATE: 08/15/2024

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## Age Requirement
- 2 years of age or older

## Baseline Clinical Evaluation
- Echocardiogram completed before starting treatment with continued monitoring as clinically appropriate [Note: Echocardiogram requirement is waived if provider, patient, and pharmacy are enrolled in the Fintepla Risk Evaluation and Mitigation Strategy (REMS) program]

## Alternative Therapies
- **Dravet Syndrome:**
  - Failure (trial for at least three months duration), contraindication, intolerance to **ONE** of the following:
    1. Valproate combined with clobazam
    2. Valproate combined with topiramate
- **Lennox Gastaut Syndrome:**
  - Failure (trial for at least three months duration), contraindication, intolerance to **ONE** of the following:
    1. Valproate combined with lamotrigine
    2. Valproate combined with rufinamide

## Brand Specific Criteria
- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

## Safety
- No FDA labeled contraindications, including concomitant use of monoamine oxidase inhibitors or within 14 days of their administration
- Does not have estimated glomerular filtration rate less than 15 milliliters per minute per 1.73 square meters (as determined by Modification of Diet in Renal Disease (MDRD))
- Individuals with moderate to severe hepatic impairment (Child Pugh Class B or C) will not be prescribed fluphenazine with clobazam and Diacomit (stiripentol)

## Documentation Requirements
- A completed request form must be submitted, including:
  - Chart notes
  - Lab results (including echocardiogram and renal function values)
  - Supporting clinical documentation

## Initial Therapy Criteria Approval Duration:
- 6 months OR end of plan year

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## Criteria for Continuation of Therapy (renewal therapy):

**Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy**

### Prescriber Qualifications

- Continues to be seen by a Neurologist or is in consultation with a Neurologist

### Indication

- Seizures associated with Dravet syndrome on stable antiepileptic medication therapy
- Seizures associated with Lennox Gastaut syndrome on stable antiepileptic medication therapy

### Clinical Response

- Positive clinical response defined as **ONE** of the following:
  - Achieved and maintains a reduction in frequency of seizures
  - Longer interval between seizures compared to baseline

### Adherence

- Adherence to the prescribed therapy regimen has been documented

### Brand Specific Criteria

- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

### Safety

- No new contraindications or significant adverse drug effects including:
  - Concomitant use of monoamine oxidase inhibitors or within 14 days of their administration
  - Serotonin syndrome
  - Valvular heart disease
  - Pulmonary arterial hypertension
  - Suicidal thoughts or behaviors
  - Acute decreases in visual acuity or ocular pain
- Does not have estimated glomerular filtration rate less than 15 milliliters per minute per 1.73 square meters (as determined by Modification of Diet in Renal Disease (MDRD))
- Individuals with moderate to severe hepatic impairment (Child Pugh Class B or C) will not be prescribed fluphenazine with clobazam and Diacomit (stiripentol)

### Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in seizure control
- Lab values confirming safe use

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**Continuation Therapy Criteria Approval Duration:**

- 12 months OR end of plan year

## Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications

2. Off-Label Use of Cancer Medications

## Description:

Fintepla (fenfluramine) 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.

The mechanisms by which fenfluramine exerts its therapeutic effects in the treatment of seizures associated with DS are unknown. Fenfluramine and the metabolite, norfenfluramine, increase extracellular levels of serotonin through interaction with serotonin transporter proteins, and exhibit agonist activity at serotonin 5HT-2 receptors.

DS, previously known as severe myoclonic epilepsy of infancy, is a rare early-onset epileptic encephalopathy characterized by refractory epilepsy and neurodevelopmental problems beginning in infancy. Patients present in the first year of life with a prolonged, often febrile, clonic seizure in the setting of normal cognitive and motor development prior to seizure onset. In most, febrile, and afebrile seizures, including episodes of status epilepticus, recur repeatedly in the weeks to months after the initial event, and psychomotor impairment begins thereafter. Myoclonus, both epileptic and non-epileptic, occurs frequently. The majority of older children and young adults with DS have motor system dysfunction, gait and postural abnormalities, and cognitive and behavioral impairment.

DS seizures tend to be refractory to most anti-seizure drugs, and some patients derive benefit from a ketogenic diet and vagus nerve stimulation. The most commonly used anti-seizure drugs include valproate, clobazam, topiramate, levetiracetam, stiripentol, and cannabidiol. Most patients require two or more agents to achieve reasonable seizure control.

Valproate is considered a first-line agent for DS with clobazam added as a second agent if valproate does not control seizures despite adequate valproate dosing and serum levels. Topiramate is a broad spectrum antiseizure agent that is also used as added on therapy. Stiripentol and fenfluramine are also considered as add-on therapy. Clonazepam, levetiracetam, zonisamide, ethosuximide, and vagal nerve stimulation are considered third-line treatments for DS. Cannabidiol is also approved for treatment for DS.

LGS, also known as Lennox syndrome, is a severe and difficult-to-treat form of childhood-onset epilepsy that commonly appears between the second and sixth year of life. It is characterized by recurrent seizures and can include different seizure types, such as, tonic, atonic, atypical absence, and myoclonic seizures. There may be periods of recurrent seizures mixed with brief, relatively seizure-free periods. Most children with LGS experience

some degree of intellectual impairment or processing of information, along with developmental delays, and behavioral disturbances.

Criteria for the diagnosis of LGS require the presence of tonic seizures and at least one additional seizure type, an EEG showing generalized slow spike-and-wave complexes of ≤2.5 Hz and generalized paroxysmal fast activity in sleep, onset before age 18 years, and long-term outcome of drug-resistant epilepsy and intellectual disability.

The first-line antiseizure medication for LGS is valproate. Nearly all patients require adjunctive antiseizure medication therapy (e.g., valproate combined with lamotrigine or rufinamide). Other treatment for LGS includes anti-epileptic medications such as clobazam, clonazepam, cannabidiol, felbamate, fenfluramine, or topiramate. There is no single antiepileptic medication that will control seizures. Children who improve initially may later show tolerance to a drug or have uncontrollable seizures.

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**Definitions:**

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

**Risk Evaluation and Mitigation Strategy (REMS) Program:**
Use of Fintepla (fenfluramine) is subject to a Risk Evaluation and Mitigation Strategies (REMS) program that requires provider, patient, and dispensing pharmacy be enrolled into the program. Only providers and Pharmacies enrolled into the REMS may prescribe and dispense the drug, respectively, to individuals who are also in the program. A REMS program attempts to manage known or potentially serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) for some drugs to ensure that the benefits of a drug outweigh its risks.

Because of the risk for valvular heart disease and pulmonary arterial hypertension, Fintepla (fenfluramine) is available through a restricted REMS program
Requirements of the Fintepla (fenfluramine) REMS Program include the following:

- Prescribers must be certified by enrolling in the REMS program
- Prescribers must counsel patients receiving Fintepla (fenfluramine) 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 (fenfluramine) treatment, and cardiac monitoring after treatment
- Patients must enroll in the REMS program and comply with ongoing monitoring requirements
- The pharmacy must be certified by enrolling in the REMS program and must only dispense to patients who are authorized to receive Fintepla (fenfluramine)
- Wholesalers and distributers must only distribute to certified pharmacies

**Modification of Diet in Renal Disease (MDRD):**
GFR in mL/min per 1.73 $m^2$ = 175 x $SerumCr^{-1.154}$ x $age^{-0.203}$ x 1.212 (if patient is black) x 0.742 (if female)

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## Resources:

Fintepla (fenfluramine) oral solution product information, revised by UCB, Inc. 01-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed April 11, 2025.

Andrade DM, Nascimento FA. Dravet syndrome: Management and prognosis. In: UpToDate, Nordli DR, Dashe JF (Eds), UpToDate, Waltham, MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through May 2025. Topic last updated March 18, 2025. Accessed June 13, 2025.

Wilfong A. Lennox-Gastaut syndrome. In: UpToDate, Nordli DR, Dashe JF (Eds), UpToDate, Waltham, MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through May 2025. Topic last updated June 10, 2025. Accessed June 13, 2025.

Brigo F, Jones K, Eltze C, Matricardi S. Anti-seizure medications for Lennox-Gastaut syndrome. Cochrane Database Syst Rev 2021; 4:CD003277. Accessed June 23, 2023. Re-evaluated June 13, 2025.

Wirrell EC, Hood V, Knupp KG, et al.: International consensus on diagnosis and management of Dravet syndrome. Epilepsia 2022; 63:1761. Accessed June 23, 2023. Re-evaluated June 13, 2025.

Montouris G, Aboumatar S, Burdette D, et al.: Expert opinion: Proposed diagnostic and treatment algorithms for Lennox–Gastaut syndrome in adult patients. Epilepsy & Behavior 110 (2020) https://doi.org/10.1016/j.yebeh.2020.107146. Accessed June 23, 2023. Re-evaluated June 13, 2025.