Clinical Policy: Fenfluramine (Fintepla)
Reference Number: CP.PMN.246
Effective Date: 09.01.20
Last Review Date: 08.20
Line of Business: Commercial, HIM, Medicaid

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) 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 (must meet all):
   1. Diagnosis of DS;
   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. 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 – Length of Benefit

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.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy
A. Dravet 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 – Length of Benefit

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.PHAR.21 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.PHAR.21 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

   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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/ Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diacomit® (stiripentol)</td>
<td>50 mg/kg/day PO in 2-3 divided doses</td>
<td>50 mg/kg/day</td>
</tr>
<tr>
<td>Epidiolex® (cannabidiol)</td>
<td>Initial: 2.5 mg/kg PO BID</td>
<td>20 mg/kg/day</td>
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<tr>
<td></td>
<td>Maintenance: 5 mg/kg PO BID</td>
<td></td>
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<tr>
<td>clobazam (Onfi®, Sympazan®)</td>
<td>Initial: 0.2-0.3 mg/kg/day PO*</td>
<td>0.5-2 mg/kg/day</td>
</tr>
<tr>
<td>Drug Name</td>
<td>Dosing Regimen</td>
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<tr>
<td>valproic acid (Depakene®, Depakote®, Stavzor®)</td>
<td>Initial: 10-15 mg/kg/day PO, given in 2-3 equally divided doses*</td>
<td>25-60 mg/kg/day</td>
</tr>
<tr>
<td>topiramate (Topamax®, Trokendi® XR, Qudexy® XR)</td>
<td>Initial: 0.5-2 mg/kg/day PO*</td>
<td>8-12 mg/kg/day</td>
</tr>
<tr>
<td>levetiracetam (Spritam®, Keppra®)</td>
<td>Initial: 10-20 mg/kg/day PO, divided in 2-3 doses*</td>
<td>60-80 mg/kg/day</td>
</tr>
<tr>
<td>Other antiepileptic drugs: clonazepam (Klonopin®), zonisamide (Zonegran®), ethosuximide (Zarontin®), phenobarbital</td>
<td>PO; off-label dosing information not available</td>
<td>Off-label dosing information not available</td>
</tr>
</tbody>
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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 of, 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):

<table>
<thead>
<tr>
<th>North American Consensus Panel</th>
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</thead>
<tbody>
<tr>
<td><strong>1st line</strong></td>
</tr>
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</table>
|  | *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 |

V. Dosage and Administration

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

VI. Product Availability
- Oral solution: 2.2 mg/mL
VII. References

Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Policy created</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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<tbody>
<tr>
<td></td>
<td>07.14.20</td>
<td>08.20</td>
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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.

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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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