Clinical Policy: Benzodiazepine Use in Pediatric Seizure Disorders
Reference Number: GA.PMN.08
Effective Date: 03/01/16
Last Review Date: 2/19
Line of Business: Medicaid

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

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® medical policy for the use of Clonazepam (Klonopin®) in pediatric seizure disorders.

FDA Approved Indication(s)
Klonopin is indicated for:
• Seizure disorders
• Panic disorder

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 Klonopin is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Absence Seizures (must meet all):
      1. Diagnosis of childhood absence epilepsy, juvenile absence epilepsy, or absence type seizures;
      2. Prescribed by or in consultation with a neurologist;
      3. Failure of a 4-week trial of two separate monotherapy of PDL agents (Valproic acid, Ethosuximide, Lamotrigine) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
      4. Failure of a 4-week trial of one combination (at least 2) of PDL agents (Valproic acid, Ethosuximide, Lamotrigine) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
      5. Dose does not exceed:
         a. Infants/children < 10 years (≤ 30kg): 0.1-0.2 mg/kg/day in three divided doses;
         b. Adolescents > 30 kg: 20mg/day in three divided doses.

   Approval duration: 3 months

   B. Myoclonic Type Seizures (must meet all):
      1. Diagnosis of myoclonic seizures;
      2. Prescribed by or in consultation with a neurologist;
3. Failure of a 4-week trial of two separate monotherapy of PDL agents (Valproic acid, Levetiracetam, Topiramate) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;

4. Failure of a 4-week trial of one combination (at least 2) of PDL agents (Valproic acid, Levetiracetam, Topiramate) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;

5. Dose does not exceed:
   a. Infants/Children < 10 years (≤ 30kg): 0.1-0.2 mg/kg/day in three divided doses;
   b. Adolescents > 30 kg: 20mg/day in three divided doses.

Approval duration: 3 months

C. Juvenile Myoclonic Epilepsy (must meet all):
   1. Diagnosis of juvenile myoclonic epilepsy;
   2. Prescribed by or in consultation with a neurologist;
   3. Failure of a 4-week trial of two separate monotherapy of PDL agents (Valproic acid, Lamotrigine, Levetiracetam or Topiramate) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   4. Failure of a 4-week trial of one combination (at least 2) of PDL agents (Valproic acid, Lamotrigine, Levetiracetam, Topiramate) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   5. Dose does not exceed:
      a. Infants/Children < 10 years (≤ 30kg): 0.1-0.2 mg/kg/day in three divided doses;
      b. Adolescents > 30 kg: 20mg/day in three divided doses.

Approval duration: 3 months

D. Lennox-Gastaut Syndrome (must meet all):
   1. Diagnosis of Lennox-Gastaut syndrome;
   2. Prescribed by or in consultation with a neurologist;
   3. Failure of a 4-week trial of Valproic acid at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   4. Failure of a 4-week trial of one combination of Valproic acid plus Lamotrigine, or Topiramate at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   5. Dose does not exceed:
      a. Infants/Children < 10 years (≤ 30kg): 0.1-0.2 mg/kg/day in three divided doses;
      b. Adolescents > 30 kg: 20mg/day in three divided doses.

Approval duration: 3 months

II. Continued Therapy

A. All Indications in Sections I (must meet all):
   1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   2. Member is responding positively to therapy as evidenced by significant reduction in seizures and not having any intolerable side effects/contraindications;
   3. If request is for a dose increase, new dose does not exceed:
      a. Infants/Children < 10 years (≤ 30kg): 0.1-0.2 mg/kg/day in three divided doses;
b. Adolescents > 30 kg: 20mg/day in three divided doses. 

**Approval duration: 6 months**

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

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*
- FDA: Food and Drug Administration
- PDL: preferred drug list

*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>
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<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/ Maximum Dose</th>
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| Ethosuximide (Zarontin®) | • Age 3-6 years: 250mg per day  
• > 6 years: 500mg per day | 1.5 gram/day |
| Lamotrigine (Lamictal®) | • Age 2-12 years: 0.15 – 15 mg/kg/day  
• >12 years: 300-500 mg/day | • 400mg/day  
• 500mg/day |
| Levetiracetam (Keppra®) | • Age 4-16 years: 20-60 mg/kg  
• ≥16 years: 1000-3000mg/day | 3000 mg/day |
| Topiramate (Topamax®) | Specific titration and dosing regimen varies based on indications, age, weight | Varies |
| Valproic acid (Depakene®) | Initiate at 10-15mg/kg/day and increase by 5-10 mg/kg/week | 60 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.*

*Appendix C: General Information*

Absence type seizures or epilepsy syndromes manifest with motionless staring, behavioral arrest, automatisms, and spikes and wave discharges on EEG. Mild facial jerks and lack of post-ictal periods are common. Absence seizures last 5-10 seconds and may cluster. Myoclonic type seizures or epilepsy syndromes display characteristic rapid, lightning like jerking movements of the whole body. It can either occur on one side or both sides of the body and may involve small or larger muscle groups.

Lennox-Gastaut syndrome is a pharmaco-resistant epileptic syndrome that starts in children less than 5 years old. Multiple seizure types, mental regression, and specific EEG patterns are characteristic of this childhood syndrome. Some recognized causes include: brain injuries or malformations, infections, and perinatal causes.
V. Dosage and Administration

<table>
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<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
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<tr>
<td>Seizures disorders</td>
<td>• Infants/Children &lt; 10 years (≤ 30kg): 0.1-0.2 mg/kg/day in three divided doses; • Adolescents &gt; 30 kg: 20mg/day in three divided doses</td>
<td>Varies</td>
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VI. Product Availability

Tablets: 0.5mg, 1mg, 2 mg

VII. References


Reviews, Revisions, and Approvals

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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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