

## Clinical Policy: Benzodiazepine Use in Pediatric Seizure Disorders

Reference Number: GA.PMN.08

Effective Date: 03/01/16

Last Review Date: 4/2021

Line of Business: Medicaid

[Revision Log](#)

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 Peach State Health Plan medical policy for the use of Clonazepam (Klonopin®) and Diazepam (Diastat®) rectal gel in pediatric seizure disorders.

### FDA Approved Indication(s)

Klonopin is indicated for:

- Seizure disorders
- Panic disorder

Diastat is indicated for:

- Seizure disorders, adjunct treatment

### 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 Peach State Health Plan that Klonopin is **medically necessary** when the following criteria are met:

#### I. Initial Approval Criteria

##### A. Generalized non-motor (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 ( $\leq$  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. Generalized other motor (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 ( $\leq$  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 ( $\leq$  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 ( $\leq 30$ kg): 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**

**E. Rescue Treatment for Acute Seizures in children Less than 2 years**

1. Diagnosis of a neurological condition that may precipitate acute seizures
2. Prescribed by or in consultation with a pediatrician or neurologic specialist
3. Age less than 2 years old
4. Documentation that treatment is intended for outpatient (home or school) rescue administration
5. Medication prescribed is generic diazepam (Diastat®) rectal gel
6. Dose does not exceed 0.5mg/kg rounded upward to next available dose

**Approval duration: 6 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 **OR**  
For Diastat, member has experienced seizures that has warranted use of on-hand doses or medication expired
3. If request is for a dose increase, new dose does not exceed  
For Clonazepam:
  - a. Infants/Children < 10 years ( $\leq 30$ kg): 0.1-0.2 mg/kg/day in three divided doses;
  - b. Adolescents > 30 kg: 20mg/day in three divided doses.For Diastat: Max 0.5mg/kg rounded upward to next available dose

**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.*

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Ethosuximide (Zarontin®)	<ul style="list-style-type: none"> <li>Age 3-6 years: 250mg per day</li> <li>&gt; 6 years: 500mg per day</li> </ul>	1.5 gram/day
Lamotrigine (Lamictal®)	<ul style="list-style-type: none"> <li>Age 2-12 years: 0.15 – 15 mg/kg/day</li> <li>&gt;12 years: 300-500 mg/day</li> </ul>	<ul style="list-style-type: none"> <li>400mg/day</li> <li>500mg/day</li> </ul>
Levetiracetam (Keppra®)	<ul style="list-style-type: none"> <li>Age 4-16 years: 20-60 mg/kg</li> <li>≥16 years: 1000-3000mg/day</li> </ul>	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.
- On September 23, 2020, the U.S. Food and Drug Administration announced in a Drug Safety Communication that it is requiring an update to the Boxed

Warning, and requiring class-wide labeling changes for benzodiazepines to include the risks of abuse, misuse, addiction, physical dependence and withdrawal reactions to help improve their safe use. The FDA is also requiring revisions to the existing patient Medication Guides for these medicines to help educate patients and caregivers about these risks.

Other changes are also being required to several sections of the prescribing information, including to the Warnings and Precautions, Drug Abuse and Dependence, and Patient Counseling Information sections.

## V. Dosage and Administration

### Clonazepam

Indication	Dosing Regimen	Maximum Dose
Seizures disorders	<ul style="list-style-type: none"> <li>Infants/Children &lt; 10 years (<math>\leq</math> 30kg): 0.1-0.2 mg/kg/day in three divided doses;</li> <li>Adolescents &gt; 30 kg: 20mg/day in three divided doses</li> </ul>	Varies

## VI. Product Availability

### Clonazepam

- Tablets: 0.5mg, 1mg, 2 mg

### Diazepam

- Rectal gel: 2.5mg Twin Pack
- Rectal gel: 10mg AcuDial Delivery System Twin Pack
  - Delivers: 5, 7.5, 10mg
- Rectal gel: 20mg AcuDial Delivery System Twin Pack
  - Delivers: 12.5, 15, 17.5, 20mg

## VII. References

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- Rijkevorsel K. Treatment of Lennox-Gastaut syndrome: overview and recent findings. *Neuropsychiatric Disease and Treatment* 2008;4(6) 1001–1019.
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- Diastat® Prescribing Information. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; December 2016. Available at:

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[https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2016/020648s014lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/020648s014lbl.pdf). Accessed September 15, 2020.

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	03.01.16	03.16
4Q 2017 annual review: no significant changes	12.01.17	12.17
1Q 2018 annual review: no significant changes	04.01.18	04.18
4Q 2018 annual review: no significant changes	12.01.18	12.18
Changed current Georgia policy templates to corporate standard templates for drug coverage criteria to meet corporate compliance. Changes/revisions included; new formatting, font size, use of standard policy language for each section of policy, and rearranged order of certain steps in criteria and sections.	2/21/19	
Annual review. Updated fonts.	3/19	4/19
Annual review. Updated classification of seizures based on International League Against Epilepsy (ILAE). Updated references.	4/2020	4/2020
Changed verbiage from Centene to Peach State Health Plan. Changed Centene logo to PSHP logo as this is a health plan specific policy. Added criteria for treatment of acute seizures with Diastat® rectal gel. Added FDA new Safety requirements for Benzodiazepines. Updated references.	10/2020	10/2020
Annual review. No changes made.	4/2021	4/2021

**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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**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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