Clinical Policy: Benzodiazepine Use in Pediatric Seizure Disorders

Reference Number: GA.PMN.08
Effective Date: 03/01/16
Last Review Date: 4/2020
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 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. 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 (≤ 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 (≤ 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.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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

Indication	Dosing Regimen	Maximum Dose
Seizures disorders	• Infants/Children < 10 years (≤ 30kg): 0.1-0.2 mg/kg/day in three divided doses; • Adolescents > 30 kg: 20mg/day in three divided doses	Varies

VI. Product Availability
Tablets: 0.5mg, 1mg, 2 mg

VII. References
1. National Institute of Health and Clinical Excellence (NICE) (2012) Epilepsies: diagnosis and management. [Online]. Available at: https://www.nice.org.uk/guidance/cg137. Accessed August 26, 2016.
2. Clinical Pharmacology. Gold Standard, Inc. Clonazepam. Available at: https://www.clinicalpharmacology.com. Accessed August 26, 2016.
3. Schmidt D, Bourgeois B. A risk-benefit assessment of therapies for Lennox-Gastaut syndrome. Drug Safety 2000;22(6):467-477. doi:10.2165/00002018-200022060-00005.
4. Rijckevorsel K. Treatment of Lennox-Gastaut syndrome: overview and recent findings. Neuropsychiatric Disease and Treatment 2008;4(6) 1001–1019.
5. Fisher et al. Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia doi: 10.111/epi.13671.

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

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.