Clinical Policy: Cannabidiol (Epidiolex)

Reference Number: CP.PMN.164
Effective Date: 09.01.18
Last Review Date: 08.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Revision Log

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

Description

Cannabidiol (Epidiolex®) is a cannabinoid.

FDA Approved Indication(s)

Epidiolex is indicated for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS), or tuberous sclerosis complex (TSC) in patients 1 year of age and older.

Policy/Criteria

Provider attestation that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Epidiolex is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Seizures Associated with Dravet Syndrome, Lennox-Gastaut Syndrome, or Tuberous Sclerosis Complex (must meet all)**:**

1. Diagnosis of DS, LGS, or TSC;
2. Age ≥ 1 year;
3. Will be used as adjunctive therapy (*see Appendix B*) with at least one other antiepileptic drug (AED);
   **For Illinois HIM requests, the step therapy requirement above does not apply as of 1/1/2026 per IL HB 5395*
4. For LGS, member meets one of the following (a or b):
   a. Request is for the treatment of a member in a State with limitations on step therapy in certain settings (*see Appendix E*);
   b. Failure of two of the following, unless clinically significant adverse effects are experienced or all are contraindicated: clobazam, clonazepam, felbamate, lamotrigine, rufinamide, topiramate;
   **For Illinois HIM requests, the step therapy requirement above does not apply as of 1/1/2026 per IL HB 5395*
5. Dose does not exceed any of the following (a or b):
   a. For DS or LGS: 20 mg/kg per day;
   b. For TSC: 25 mg/kg per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Seizures Associated with Dravet Syndrome, Lennox-Gastaut Syndrome, or Tuberous Sclerosis Complex (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Epidiolex for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Epidiolex will continue to be used as adjunctive therapy (*see Appendix B*) with at least one other AED;
   **For Illinois HIM requests, the step therapy requirement above does not apply as of 1/1/2026 per IL HB 5395*
4. If request is for a dose increase, new dose does not exceed any of the following (a or b):
   a. For DS or LGS: 20 mg/kg per day;
   b. For TSC: 25 mg/kg per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, 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.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AED: antiepileptic drug
DS: Dravet syndrome
FDA: Food and Drug Administration
LGS: Lennox-Gastaut syndrome
TSC: tuberous sclerosis complex

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
LGS, DS		
topiramate (Topamax®, Qudexy® XR)	**LGS** • Adults and Adolescents 17 years and older: Initial dose is 25 to 50 mg/day orally. Maintenance dose is 200 to 400 mg/day orally (divided and given twice daily). • Children and Adolescents 2 to 16 years: Initial dose is 1 to 3 mg/kg/day (max: 25 mg/day) orally once daily in the evening. Maintenance dose is 5 to 9 mg/kg/day orally. **DS**‡ Initial dose is 0.5 to 2 mg/kg/day orally. Max target dose is 8 to 12 mg/kg/day orally.	LGS: Age ≥ 17: 400 mg/day Age 2 – 16: 25 mg/day DS: 8 to 12 mg/kg/day
lamotrigine (Lamictal® CD, ODT, XR, & Subvenite®)	**LGS**‡ • Patients receiving enzyme-inducing AEDs (e.g., carbamazepine, phenobarbital, phenytoin, primidone) NOT to include valproate: ○ Adults and Adolescents: Initial dose is 50 mg orally daily. Maintenance dose is 300 to 500 mg/day orally given in 2 divided doses.	With valproate: 100 mg/day With enzyme-inducing drugs: 400 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	○ Children 2 to 12 years: Initial dose is 0.6 mg/kg/day orally in 2 divided doses. Maintenance dose is 5 to 15 mg/kg/day (max 400 mg/day) orally given in 2 divided doses. • Patients receiving valproate: ○ Adults and Adolescents: Initial dose is 25 mg orally every other day is given for 2 weeks. Maintenance dose is 100 to 400 mg/day orally, given in 1 to 2 divided doses. ○ Children 2 to 12 years: Dosage depends on weight. **DS**[ǂ] Avoid lamotrigine and other sodium channel agents since they can exacerbate seizures associated with Dravet Syndrome.	
felbamate (Felbatol®)	**LGS** Adolescents and Children 2 - 14 years: Add felbamate at 15 mg/kg/day orally in 3-4 divided doses while reducing doses of other AEDs by 20-30%. Increase felbamate dose by 15 mg/kg/day increments at weekly intervals to 45 mg/kg/day orally. Max dose is 3,600 mg/day orally.	3,600 mg/day
rufinamide (Banzel®)	**LGS** • Adults and Adolescents ≥ 17 years: Initial dose is 400-800 mg/day orally in 2 equally divided doses. Target and max dose is 3,200 mg/day orally given in 2 equally divided doses. • Children and Adolescents 1-16 years: Initial dose is 10 mg/kg/day orally given as 2 equally divided doses. Maintenance target dose is 45 mg/kg/day or 3,200 mg/day orally, whichever is less, given in 2 equally divided doses. **DS** Avoid rufinamide and other sodium channel agents since they can exacerbate seizures associated with Dravet Syndrome.	3,200 mg/kg/day
clobazam (Onfi®)	**LGS** For Adults, Adolescents, & Children older than 2 years: • Patients weighing > 30 kg: Initial dose is 5 mg orally twice daily. Max dose is 20 mg orally twice daily. Dosing should be individualized based upon efficacy and tolerability.	LGS: ≤ 30 kg: 0.2 mg/kg/day > 30 kg: 20 mg/day DS: 2 mg/kg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	• Patients weighing ≤ 30 kg: Initial dose is 5 mg orally once daily. Max dose is 10 mg orally twice daily. Dosing should be individualized based upon efficacy and tolerability. **DS**‡ Initial dose is 0.2 to 0.3 mg/kg/day PO. Max target dose is 0.5 to 2 mg/kg/day PO.	
clonazepam (Klonopin®)	**LGS** For Adults, Adolescents, & Children: • Patients weighing > 30 kg: Initial dose is 1.5 mg/day orally, given in three equally divided doses. Max dose is 20 mg/day orally, given in three equally divided doses. • Patients weighing ≤ 30 kg: Initial dose is 0.01 to 0.03 mg/kg/day orally, given in three equally divided doses. Max dose is 0.1 to 0.2 mg/kg/day orally, given in three equally divided doses.	≤ 30 kg: 0.2 mg/kg/day > 30 kg: 20 mg/day
valproic acid (Depakene®, Depakote®, Stavzor®)	**LGS**‡ Initial dose is 7 to 10 mg/kg/day PO, given three to four times daily for nonenteric-coated capsules or syrup, BID for delayed-release tablets, and QD for the extended release preparation. A typical adult starting dose is 500 mg QD. The max dose is 60 mg/kg/day or 3,000 mg/day. **DS**‡ Initial dose is 10 to 15 mg/kg/day PO, given in two to three equally divided doses. Max target dose is 25 to 60 mg/kg/day PO, given in two to three equally divided doses, depending on achieved blood levels.	LGS: 60 mg/kg/day or 3,000 mg/day DS: 60 mg/kg/day
levetiracetam (Spritam®, Keppra®)	**LGS**‡ Initial dose is 5 mg/kg/day PO, given in two or three equal doses per day. Max dose is 20 to 80 mg/kg/day PO, according to effectiveness and tolerability. **DS**‡ Initial dose is 10 to 20 mg/kg/day PO, divided twice daily or three times daily. Max dose is 60 to 80 mg/kg/day PO, divided twice daily or three times daily.	80 mg/kg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
TSC		
AED examples for partial seizures	carbamazepine (Tegretol®), felbamate (Felbatol®), gabapentin (Neurontin®), lamotrigine (Lamictal®), levetiracetam (Keppra®), oxcarbazepine (Trileptal®), phenytoin (Dilantin®), tiagabine (Gabitril®), topiramate (Topamax®), valproic acid (Depakene®), divalproex sodium (Depakote®), vigabatrin (Sabril®), zonisamide (Zonegran®)	Varies according to the agent used
AED examples for generalized onset seizures	carbamazepine (Tegretol®), lamotrigine (Lamictal®), levetiracetam (Keppra®), phenytoin (Dilantin®), primidone (Mysoline®), topiramate (Topamax®), valproic acid (Depakene®), divalproex sodium (Depakote®)	Varies according to the agent used
Afinitor Disperz® (everolimus)	**TSC-associated partial-onset seizures** 5 mg/m^2 PO QD; adjust dose to attain trough concentration of 5-15 ng/mL	Based on trough concentration

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.
ǂ *Off-label*

Appendix C: Contraindications / Boxed Warnings

- Contraindication(s): hypersensitivity to cannabidiol or any of the ingredients in the product
- Boxed warning(s): none reported

Appendix D: General Information

- DS, also called severe myoclonic epilepsy of infancy, is a severe form of epilepsy. Per the United Kingdom National Institute for Health and Care Excellence (NICE) Anti-Epileptic Pharmacologic Treatment Guidelines (published on January 2012 and updated on April 2018), the recommended first-line anti-epileptic drugs to treat DS are sodium valproate and topiramate. Clobazam and stiripentol are listed as adjunctive anti-epileptic drugs. Except for stiripentol, these drugs are not FDA-approved for treatment of DS.
- LGS is another severe form of epilepsy. Per American Academy of Neurology and the American Epilepsy Society Anti-Epileptic Pharmacologic Treatment Guidelines, the recommended treatment for drop seizures associated with LGS is lamotrigine and topiramate (Level A).
    - A Cochrane Database of Systematic Review 2013 article concluded that the optimum treatment for LGS remains uncertain and no study to date has shown any one drug to be highly efficacious; rufinamide, lamotrigine, topiramate and felbamate may be helpful as add-on therapy, and clobazam may be helpful for drop seizures. Until further research has been undertaken, clinicians will need to continue to consider each patient individually, taking into account the potential benefit of each therapy weighed against the risk of adverse effects.

- Seizures associated with TSC are a rare neurocutaneous genetic disorder, with a prevalence of one in 6,000 to 10,000. Mutations in either TSC1 or TSC2 lead to over-activation of the mammalian target of rapamycin (mTOR) pathway and relatively uncontrolled cell growth that causes growth of benign tumors (hamartomas) in various organs, such as the brain, kidneys, skin, heart, lungs and bones, with epilepsy being the most common neurological symptom in TSC. While vigabatrin is the recommended first-line therapy for TSC-associated infantile spasms, anticonvulsant therapy of other seizure types in TSC should generally follow that of other epilepsies per the Tuberous Sclerosis Complex Surveillance and Management Recommendations of the 2012 International Tuberous Sclerosis Complex Consensus Conference and the 2019 UK guidelines for management and surveillance of TSC. Patients with TSC can present with almost any seizure type including tonic, atonic or tonic-clonic seizures, with about two-thirds having refractory focal-onset (previously referred to as partial-onset) epilepsy; focal seizures and epileptic spasms are the most prevalent.

Appendix E: States with Limitations against Redirections in Certain Settings

State	Step Therapy Prohibited?	Notes
NV	No	**Applies to Medicaid requests only** Failure of ONE of the following, unless clinically significant adverse effects are experienced or all are contraindicated: clobazam, clonazepam, felbamate, lamotrigine, rufinamide, topiramate.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
DS, LGS	Initial dose is 2.5 mg/kg PO BID (5 mg/kg/day). Maintenance dose is 5 mg/kg PO BID (10 mg/kg/day) to 10 mg/kg PO BID (20 mg/kg/day). Dosage adjustment is recommended for patients with moderate or severe hepatic impairment.	20 mg/kg/day
TSC	Initial dose is 2.5 mg/kg PO BID (5 mg/kg/day). Increase the dose in weekly increments of 2.5 mg/kg PO BID (5 mg/kg/day), as tolerated, to a recommended maintenance dosage of 12.5 mg/kg PO BID (25 mg/kg/day). For patients in whom a more rapid titration to 25 mg/kg/day is warranted, the dosage may be increased no more frequently than every other day.	25 mg/kg/day

VI. Product Availability

Oral solution: 100 mg/mL (60 mL, 100 mL)

VII. References

1. Epidiolex Prescribing Information. Carlsbad, CA: Greenwich Biosciences, Inc; July 2025. Available at: https://pp.jazzpharma.com/pi/epidiolex.en.USPI.pdf. Accessed April 7, 2026.
2. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed June 5, 2024.
3. Wirrell EC, Hood V, Knupp KG, et al. International consensus on diagnosis and management of Dravet syndrome. Epilepsia. February 2022;63:1761-77.
4. Ferrie CD, Patel A. Treatment of Lennox-Gastaut syndrome. Eur J Paediatr Neurol. 2009 Nov;13(6):493-504.
5. Kanner AM, Ashman E, Gloss D, et al. Practice guideline update summary: Efficacy and tolerability of the new antiepileptic drugs II: Treatment resistant epilepsy. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Epilepsy Society. July 10, 2018; 91 (2).
6. Asadi-Pooya AA. Lennox-Gastaut syndrome: a comprehensive review. Neurol Sci. 2018 Mar;39(3):403-414. doi: 10.1007/s10072-017-3188-y. Epub 2017 Nov 9. https://www.ncbi.nlm.nih.gov/pubmed/29124439.
7. Amin S, Kingswood JC, Bolton PF, et al. The UK guidelines for management and surveillance of Tuberous Sclerosis Complex. QJM: An International Journal of Medicine. 2019;112(3):171–182.
8. Northrup H, Aronow ME, Bebin EM, et al. Updated international tuberous sclerosis complex diagnostic criteria and surveillance and management recommendations. Pediatr Neurol. 2021;123:50-66.
9. Auvin S, Arzimanoglou A, Falip M, et al. Refining management strategies for Lennox-Gastaut syndrome: updated algorithms and practical approaches. Epilepsia Open. 2025;10:85–106. https://doi.org/10.1002/epi4.13075.
10. Specchio N, Nabbout R, Aronica E, et al. Updated clinical recommendations for the management of tuberous sclerosis complex associated epilepsy. European J Pediatric Neurology. 2023;47:25-34.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2022 annual review: no significant changes; references reviewed and updated.	05.12.22	08.22
Per August SDC, removed neurologist prescriber requirement. Template changes applied to other diagnoses/indications.	08.23.22	11.22
3Q 2023 annual review: no significant changes; references reviewed and updated.	05.18.23	08.23
For LGC, added redirection bypass for members in a State with limitations on step therapy in certain settings along with Appendix E, which includes Nevada with requirements for single drug redirection for Medicaid requests.	08.31.23	
Per August SDC, revised template language from requiring documentation to instead require provider attestation that member has met all approval criteria.	08.22.23	12.23

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2024 annual review: no significant changes; references reviewed and updated.	05.14.24	08.24
3Q 2025 annual review: no significant changes; added step therapy bypass for IL HIM per IL HB 5395; references reviewed and updated.	06.06.25	08.25
3Q 2026 annual review: no significant changes; added ICHRA line of business; references reviewed and updated.	04.07.26	08.26

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.

©2018 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene® and Centene Corporation® are registered trademarks exclusively owned by Centene Corporation.