Clinical Policy: Ganaxolone (Ztalmy)

Reference Number: CP.PMN.278
Effective Date: 09.01.22
Last Review Date: 05.24
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Ganaxolone (Ztalmy®) is a neuroactive steroid gamma-aminobutyric acid (GABA) A receptor positive modulator.

FDA Approved Indication(s)

Ztalmy is indicated for the treatment of seizures associated with cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD) 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 Ztalmy is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Seizures Associated with CDKL5 Deficiency Disorder (must meet all)**:**

1. Diagnosis of CDD;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 2 years;
4. Documentation of baseline monthly seizure frequency;
5. Dose does not exceed any of the following (a or b):
   a. Weight ≤ 28 kg: 63 mg/kg/day;
   b. Weight > 28 kg: 1,800 mg/day.

Approval duration: 6 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) 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, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) 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, 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, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Seizures Associated with CKDL5 Deficiency Disorder (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Ztalmy for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy (e.g., reduction in number of monthly seizures from baseline);
3. If request is for a dose increase, new dose does not exceed any of the following (a or b):
   a. Weight ≤ 28 kg: 63 mg/kg/day;
   b. Weight > 28 kg: 1,800 mg/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) 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, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) 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, 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, 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, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CDD: cyclin-dependent kinase-like 5 deficiency disorder
CDKL5: cyclin-dependent kinase-like 5
FDA: Food and Drug Administration
GABA: gamma-aminobutyric acid

Appendix B: Therapeutic Alternatives

Not applicable.

Appendix C: Contraindications/Boxed Warnings

None reported.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Seizure treatment associated with CDD	Weight ≤ 28 kg: 6 mg/kg PO TID (18 mg/kg/day) Weight > 28 kg: 150 mg PO TID (450 mg/day)	Weight ≤ 28 kg: 21 mg/kg TID (63 mg/kg/day) Weight > 28 kg: 600 mg TID daily (1,800 mg/day)

VI. Product Availability

Oral suspension: 50 mg/mL

VII. References

1. Ztalmy Prescribing Information. Radnor, PA: Marinus Pharmaceuticals, Inc; June 2023. Available at: www.ztalmyhcp.com. Accessed January 19, 2024.
2. Chin RF, Mingorance A, Ruban-Fell, et al. Treatment guidelines for rare, early-onset, treatment-resistant epileptic conditions: a literature review on dravet syndrome, lennox-gastaut syndrome and CDKL5 deficiency disorder. Front Neurol. Oct 2021; 12: 734512
3. Olson HE, Daniels CI, Haviland I, et al. Current neurologic treatment and emerging therapies in CDKL5 deficiency disorder. Journal of Neurodevelopmental Disorders. 2021. 13:40.
4. Olsen HE, Demarest ST, Prestana-Knight EM, et al. Cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder: clinical review. Pediatr Neurol. August 2019; 97: 18-25.
5. Jakimiec M, Paprocka J and Smigiel R. CDKL5 deficiency disorder – a complex epileptic encephalopathy. Brain Sc. 2020: 10 (107).
6. Amin S, Monaghan M, Aledo-Serrano A et al. International consensus recommendations for the assessment and management of individuals with CDKL5 deficiency disorder. Front Neurol. 2022 Jun 20;13:874695.
7. 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. Epilepsy Curr. Jul-Aug 2018;18(4):269-78.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	03.22.22	05.22
Template changes applied to other diagnoses/indications.	10.07.22	
2Q 2023 annual review: no significant changes; references reviewed and updated.	01.31.23	05.23
2Q 2024 annual review: revised language from "member is experiencing" to "documentation" of baseline monthly seizure frequency to help determine positive response with example added for continued therapy; references reviewed and updated.	01.19.24	05.24

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.