Clinical Policy: Ganaxolone (Ztalmy)

Reference Number: ERX.SPA.477
Effective Date: 06.01.22
Last Review Date: 05.22
Line of Business: Commercial, 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Ztalmy is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of CDD;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 2 years;
4. Member is experiencing baseline monthly seizure frequency;
5. Failure of ≥ 2 anti-seizure drugs (*see Appendix B for examples)*, unless clinically significant adverse effects are experienced or all are contraindicated;
6. Dose does not exceed any of the following (a or b):
   a. Weight ≤ 28 kg: 63 mg/kg per day;
   b. Weight > 28 kg: 1,800 mg per day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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;
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 per day;
   b. Weight > 28 kg: 1,800 mg per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 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
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Class	Examples	Dose Limit/ Maximum Dose
Anticonvulsants 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®), zonisamide (Zonegran®)	Varies according to the agent used
Anticonvulsants for tonic-clonic 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

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: Contraindications/Boxed Warnings
None reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Seizures associated with CDD	≤ 28 kg: 6 mg/kg PO TID (18 mg/kg/day)	21 mg/kg TID (63 mg/kg/day)
	> 28 kg: 150 mg PO TID (450 mg/day)	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; March 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/215904s000lbl.pdf. Accessed March 22, 2022.
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).

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	03.22.22	05.22

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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