Pharmacy Policy Bulletin: J-1222 Ztalmy (ganaxolone) – Commercial and Healthcare Reform	
Number: J-1222	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1222-004	**Original Date:** 06/01/2022
Effective Date: 07/18/2025	**Review Date:** 06/25/2025

Drugs Product(s):	• Ztalmy (ganaxolone)
FDA-Approved Indication(s):	• Treatment of seizures associated with cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD) in patients 2 years of age and older.

Background:	• Though the precise mechanism by which Ztalmy exerts therapeutic effects in CDD is unknown, its anticonvulsant effects are thought to result from positive allosteric modulation of the gamma-aminobutyric acid type A ($GABA_a$) receptor in the central nervous system. • CDD is a rare genetic condition that is caused by mutations in the CDKL5 gene, which is found on the X chromosome. Due to the location of the gene, this condition mostly affects girls, however, many cases have been identified in boys. The incidence of CDD is estimated between one in 40,000-60,000 live births, making it one of the most common genetic forms of epilepsy. The CDKL5 gene provides instructions for making a protein that is essential for normal brain and neuron development. • The most prominent feature of CDD is early-onset epilepsy. The onset of seizures can happen within the first hours, days, weeks, or months of life. Patients with CDD usually have several seizure types, with one study reporting an average of 2.8 different seizure types at any time. In addition to seizures, some of the other symptoms of CDD are developmental delays, autism, low muscle tone, apraxia, cortical blindness, scoliosis, small, cold feet, absent or limited speech, limited hand skills, feeding difficulties, and gastrointestinal problems. • Medical management for treatment of patients with CDD is mostly symptomatic and supportive. Interventions such as physical therapy, occupational therapy, visual and speech therapy, as well as augmentative communication therapy should start early. The control of seizures is often the most difficult health issue to manage. • Prescribing Considerations:

	○ Ztalmy is administered orally three times daily with food. ○ Each dose of Ztalmy must be prepared and administered using an adaptor for the Ztalmy bottle and oral dosing syringes. ○ Decrease the dose of Ztalmy gradually when discontinuing treatment. As with all antiepileptic drugs, abrupt discontinuation should be avoided, when possible, to minimize the risk of increased seizure frequency and status epilepticus. ○ Discard any unused Ztalmy oral suspension after 30 days of opening the bottle or the "Discard After" date on the bottle, whichever is sooner.

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Ztalmy may be approved when all of the following criteria are met **(A. through E.)**:

A. The member is 2 years of age and older.
B. The medication is prescribed by or in consultation with a neurologist.
C. The member has a diagnosis of CDKL5 deficiency disorder confirmed by genetic testing. (ICD-10: G40.42).
D. The member has experienced therapeutic failure or intolerance to two (2) plan-preferred antiepileptic medications.
E. The prescriber provides documentation of baseline monthly seizure frequency.

II. Reauthorization

When a benefit, reauthorization of Ztalmy may be approved when the following criterion is met **(A.)**:

A. The prescriber provides documentation of a decrease in monthly seizure frequency compared to baseline.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Ztalmy [package insert]. Radnor, PA: Marinus Pharmaceuticals, Inc.; April 2024.

2. International Foundation for CDKL5 Research. CDKL5 Disorder; An Introductory Guide. Available at: https://www.cdkl5.com/wp-content/uploads/2017/01/CDKL5_Introductory-Guide.pdf. Accessed May 02, 2025.
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.