Pharmacy Policy Bulletin

Title:	Ganaxolone (Ztalmy®)
Policy #:	Rx.01.269

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for **Ganaxolone (Ztalmy®)** as provided under the member's prescription drug benefit.

Description:

Cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD) is a rare, genetic, developmental epileptic encephalopathy characterized by early onset, treatment refractory seizures, motor impairments, and severe neurodevelopmental delays. CDD is estimated to affect 1 in 40,000 to 1 in 60,000 live births, with reported cases increasing as genetic testing becomes more common. The clinical severity of CDD is variable, and patients may experience one or more of several different seizure types, including infantile spasms (IS) and tonic-clonic, atonic, clonic, myoclonic, absence, and focal seizures. Patients with CDD generally respond poorly to currently approved drugs for varying seizure types, and there are currently no other approved treatments specifically for CDD.

The mechanism by which Ztalmy exerts its therapeutic effects in the treatment of seizures associated with CDD is unknown, but its anticonvulsant effects are thought to result from positive allosteric modulation in both the synaptic and extra synaptic gamma-aminobutyric acid-A (GABAA) receptors in the central nervous system (CNS), decreasing neuron excitability.

Ztalmy is indicated for the treatment of seizures associated with CDD in patients ≥ 2 years of age.

Policy:

INITIAL CRITERIA Ganaxolone (Ztalmy®) is approved when ALL of the following are met:

1. Diagnosis of cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD); and
2. Documentation of mutation in the CDKL5 gene; and
3. Member is experiencing motor seizures (e.g., bilateral tonic, generalized tonic-clonic, bilateral clonic, atonic, focal, or bilateral tonic-clonic); and
4. One of the following:
    a. Inadequate response or inability to tolerate two formulary anticonvulsants (e.g., valproic acid, levetiracetam, lamotrigine); or
    b. Continuation of therapy with requested medication; and
5. Member is 2 years of age or older; and
6. Prescribed by or in consultation with a neurologist

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA Ganaxolone (Ztalmy®) is re-approved when BOTH of the following are met:

1. Documentation of positive clinical response to therapy (e.g., reduction in frequency of major motor seizures compared to baseline); and

2. Prescribed by or in consultation with a neurologist

Reauthorization duration: 2 years

Black Box Warning as shown in the drug Prescribing Information:

N/A

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

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;13:874695.

Food and Drug Administration (FDA). FDA approves drug for treatment of seizures associated with rare disease in patients two years of age and older [news release]. March 18, 2022. https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-drug-treatment-seizures-associated-rare-disease-patients-two-years-age-and-older. Accessed April 19, 2023.

Food and Drug Administration. Ztalmy (ganaxolone) summary review. March 18, 2022. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2022/215904Orig1s000SumR.pdf. Accessed April 19, 2023.

Jakimiec M, Paprocka J, Śmigiel R. CDKL5 deficiency disorder-a complex epileptic encephalopathy. Brain Sci. 2020;10(2):107.

Knight EMP, Amin S, Bahi-Buisson N, et al; Marigold Trial Group. Safety and efficacy of ganaxolone in patients with CDKL5 deficiency disorder: results from the double-blind phase of a randomised, placebo-controlled, phase 3 trial. Lancet Neurol. 2022;21(5):417-427.

Leonard H, Downs J, Benke TA, et al. CDKL5 deficiency disorder: clinical features, diagnosis, and management. Lancet Neurol. 2022;21(6):563-576.

Ztalmy (ganaxolone) [package insert]. Radnor, PA: Marinus Pharmaceuticals, Inc.; November 2022. Available from: https://marinuspharma.com/wp-content/uploads/2022/03/prescribing-information.pdf. Accessed April 19, 2023.

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Ztalmy®	Ganaxolone

Cross References:

Rx.01.33 Off Label Use

Policy Version Number:	2.00
P&T Approval Date:	March 16, 2023

Policy Effective Date:	July 01, 2023
Next Required Review Date:	March 16, 2024