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Section:	Prescription Drugs	**Effective Date:**	January 1, 2024
Subsection:	Neuromuscular Agents	**Original Policy Date:**	April 15, 2022
Subject:	Ztalmy	**Page:**	1 of 4

Last Review Date: December 8, 2023

Ztalmy

Description

Ztalmy (ganaxolone) oral suspension

Background

Ztalmy (ganaxolone) is a neuroactive steroid gamma-aminobutyric acid (GABA) A receptor positive modulator. The precise mechanism by which Ztalmy exerts its therapeutic effects in the treatment of seizures associated with cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD) is unknown, but 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 (1).

Regulatory Status

FDA-approved indication: 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 (1).

Ztalmy contains warnings for somnolence, sedation and suicidal behavior and ideation (1).

Ztalmy dose should be decreased 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 (1).

The safety and effectiveness of Ztalmy in pediatric patients less than 2 years of age have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Ztalmy may be considered **medically necessary** if the conditions indicated below are met.

Ztalmy may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 2 years of age and older

Diagnosis

Patient must have the following:

Seizures associated with cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD)

AND ALL of the following:

1. Molecular confirmation of a pathogenic or likely pathogenic mutation in the CDKL5 gene
2. Inadequate response, intolerance, or contraindication to at least **TWO** antiepileptic drugs (e.g., valproate, levetiracetam, clobazam, vigabatrin, etc.)
3. Prescriber agrees to monitor for the emergence or worsening of depression, suicidal thoughts or behavior, or unusual changes in mood or behavior
4. Prescriber agrees to decrease Ztalmy dose gradually when discontinuing treatment

Prior – Approval *Renewal* Requirements

Age 2 years of age and older

Diagnosis

Patient must have the following:

Seizures associated with cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD)

AND ALL of the following:

1. Decrease in the number of seizures from baseline
2. Prescriber agrees to monitor for the emergence or worsening of depression, suicidal thoughts or behavior, or unusual changes in mood or behavior
3. Prescriber agrees to decrease Ztalmy dose gradually when discontinuing treatment

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 30 bottles (3300 mL) per 90 days

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Ztalmy (ganaxolone) is a $GABA_A$ receptor positive modulator for the treatment of seizures associated with CDKL5 deficiency disorder (CDD). Patients should be monitored for suicidal behavior and thoughts and the dose should be gradually decreased upon discontinuation to reduce the risk of increased seizure frequency. The safety and effectiveness of Ztalmy in pediatric patients less than 2 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Ztalmy while maintaining optimal therapeutic outcomes.

References

1. Ztalmy [package insert]. Radnor, PA: Marinus Pharmaceuticals, Inc.; June 2023.

Policy History

Date	Action
April 2022	Addition to PA
June 2022	Annual review
September 2022	Annual review and reference update
December 2022	Annual review
December 2023	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 8, 2023 and is effective on January 1, 2024.