SmartPA Criteria Proposal

Drug/Drug Class:	Ztalmy Clinical Edit
First Implementation Date:	TBD
Proposed Date:	December 15, 2022
Prepared for:	MO HealthNet
Prepared by:	MO HealthNet/Conduent
Criteria Status:	☐Existing Criteria ☐Revision of Existing Criteria ☒New Criteria

Executive Summary

Purpose: Ensure appropriate utilization and control of Ztalmy® (ganaxolone)

Why Issue Selected: Ztalmy® (ganaxolone), FDA approved on March 18, 2022, 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. CDD, first discovered in 2004, is a rare developmental disorder caused by pathogenic variants in the *CDKL5* gene resulting in a nonfunctional CDKL5 protein. The CDKL5 protein is involved in the proliferation, neuronal migration and formation, neuronal growth, and development and functioning of synapses during brain maturation. CDD, a form of developmental epileptic encephalopathy, is characterized by early-onset (often treatment-refractory) epilepsy, generalized hypotonia, psychomotor developmental disorders, cortical vision disorders, and significant intellectual disability. Additional symptoms may include poor social interactions, poor eye contact, hand stereotypy, vegetative disorders, gastrointestinal (i.e., constipation, gastroesophageal reflux disease) and orthopedic (i.e., scoliosis) complaints, feeding and swallowing disorders, or dysmorphic facial features. The first episodes of epileptic seizures occur in the first six weeks of life for 96% of patients and within the first three months in 90% of patients. While the pathogenic gene variants occur in approximately 1 in 40,000 to 60,000 live births and are four times more prevalent in females, the condition tends to be more severe in males, often leading to death in the first or second decade of life. Ztalmy is the first FDA approved therapy for CDD. Primary goals of therapy are to control the most problematic complaints that increase disability, increase possibility for patient development, and improve quality of life for both the patient and family.

Due to the high cost and specific approved indication, MO HealthNet will impose clinical criteria to ensure appropriate utilization of Ztalmy.

Program-Specific Information:

Drug	Cost per 110 ml bottle	Estimated annual cost for 17 kg participant
ZTALMY 50 MG/ML SUSPENSION	$2,425 WAC	$174,600

Type of Criteria:

☐ **Increased risk of ADE**
☒ **Appropriate Indications**
☐ **Preferred Drug List**
☒ **Clinical Edit**

Data Sources:

☐ **Only Administrative Databases**
☒ **Databases + Prescriber-Supplied**

Setting & Population

- Drug class for review: Ztalmy® (ganaxolone)
- Age range: All appropriate MO HealthNet participants aged 2 years or older

Approval Criteria

Initial Therapy:

- Prescribed by or in consultation with a neurologist or other specialist in the treated disease state **AND**
- Documented diagnosis of cyclin-dependent kinase-like 5 deficiency disorder (CDD) **AND**
- Documentation of genetic testing confirming presence of pathogenic or likely pathogenic variant in the *CDKL5* gene **AND**
- Participant aged 2 years or older **AND**
- Documented therapeutic trial of ≥ 2 prior antiepileptic therapies (i.e., clobazam, felbamate, lamotrigine, levetiracetam, rufinamide, topiramate, valproate, vigabatrin, cannabidiol) **AND**
- Claim does not exceed maximum dosage limitations:
  - For participants weighing ≤ 28 kg: 63 mg/kg/day
  - For participants weighing > 28 kg: 1,800 mg/day **AND**
- Documentation of baseline monthly seizure frequency
- Initial approval: 6 months

Continuation of Therapy:

- Documentation of reduced seizure burden or improvement in quality of life using a validated scale for the disease state
- Continued approval: 12 months

Denial Criteria

- Therapy will be denied if all approval criteria are not met

Required Documentation

Laboratory Results:		Progress Notes:	
MedWatch Form:		Other:	**X**

Disposition of Edit

Denial: Exception code “0682” (Clinical Edit)
Rule Type: CE

Default Approval Period

6 months

References

- Ztalmy (ganaxolone)[package insert]. Radnor, PA: Marinus Pharmaceuticals, Inc.; March 2022.
- IPD Analytics. New Drug Review: Ztalmy (ganaxolone). April 2022. Accessed April 1, 2022.

- Chin RF, Mingorance A, Ruban-Fell B, 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. 2021; 734612(12). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8573384/. Accessed April 6, 2022.
- Jakimiec M, Paprocka J, Smigiel R. CDKL5 Deficiency Disorder – A Complex Epileptic Encephalopathy. Brain Sci. 2020; 107(10). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7071516/pdf/brainsci-10-00107.pdf. Accessed April 6, 2022.
- NIH: U.S. National Library of Medicine. Study of Adjunctive Ganaxolone Treatment in Children and Young Adults with CDKL5 Deficiency Disorder (Marigold). https://www.clinicaltrials.gov/ct2/show/NCT03572933. Accessed April 6, 2022.