Effective Date **3/1/2024**
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Coverage Policy Number **IP0106**

Clobazam

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for clobazam oral soluble film (**Sympazan**®).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Clobazam oral soluble film (Sympazan) is considered medically necessary when ONE of the following is met:

1. **Lennox-Gastaut Syndrome.**
    A. Age 2 years or older
    B. Documentation of **ONE** of the following:
        i. Failure, contraindication or intolerance to at least **TWO** other antiseizure medications (for example, valproic acid, levetiracetam, zonisamide, Fycompa (perampanel), vigabatrin)

ii. Failure, contraindication or intolerance to **ONE** of the following: lamotrigine, topiramate, rufinamide, felbamate, Fintepla (fenfluramine oral solution), or Epidiolex (cannabidiol oral solution)

C. Concomitantly administered with at least one other antiseizure medication
D. Medication is prescribed by or in consultation with a neurologist

2. **Dravet syndrome.** Individual meets **ALL** of the following criteria:
   A. Age 2 years or older
   B. Medication is prescribed by or in consultation with a neurologist
   C. Documented inability to swallow **BOTH** of the following:
      i. clobazam oral suspension
      ii. clobazam tablets

3. **Treatment-Refractory Seizures/Epilepsy**
   A. Age 2 years or older
   B. Failure, contraindication or intolerance to at least **TWO** other antiseizure medications (for example, valproic acid, lamotrigine, topiramate, clonazepam, levetiracetam, zonisamide, rufinamide, felbamate)
   C. Concomitantly administered with at least one other antiseizure medication
   D. Medication is prescribed by or in consultation with a neurologist

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of clobazam oral soluble film (Sympazan) is considered medically necessary for **ALL** covered diagnoses when the above medical necessity criteria are met AND there is documentation of beneficial response (for example, reduced seizure severity, frequency and/or duration from baseline [prior to initiation of clobazam oral soluble film]).

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Background

OVERVIEW
All forms of clobazam are indicated for the adjunctive treatment of seizures associated with **Lennox-Gastaut syndrome** (LGS) in patients ≥ 2 years of age.[1,2]

Disease Overview
LGS, a severe epileptic and developmental encephalopathy, is associated with a high rate of morbidity and mortality.[3,4] LGS most often begins between 3 and 5 years of age and comprises approximately 4% to 10% of childhood epilepsies; the prevalence is 0.26 per 1,000 people.[3-6] Affected children experience several different types of seizures, most commonly atonic seizures (sudden loss of muscle tone and limpness, also called drop seizures) and tonic seizures (increased muscle tone and muscle stiffness).[3,6] Seizures associated with LGS are usually resistant to treatment.[6] The three main forms of treatment of LGS are antiseizure medications (ASMs),

dietary therapy (typically the ketogenic diet), and device/surgery (e.g., vagus nerve stimulation, corpus callosotomy).[6] None of the therapies are effective in all cases of LGS and the disorder has proven particularly resistant to most therapeutic options. The choice of treatment should take into consideration the patient's age and other associated conditions.

Other Uses with Supportive Evidence
Dravet syndrome is a rare genetic epileptic encephalopathy (dysfunction of the brain) marked with frequent and/or prolonged seizures.[7,8] It has been estimated that 1 out of 15,700 infants born in the US are affected with Dravet syndrome. The seizures generally begin in the first year of life in an otherwise healthy infant. Affected individuals can develop many seizure types: myoclonic, tonic-clonic, absence, atypical absence, atonic, focal aware or impaired awareness (previously called partial seizures), and status epilepticus.[8] As the seizures continue, most of the children develop some level of developmental disability and other conditions associated with the syndrome. Two or more ASMs are often needed to control the seizures; most of the seizures are refractory to medications. The goals of treatment are cessation of prolonged convulsions, reductions in overall seizure frequency, and minimization of treatment side effects.[9,10] Some patients respond to the ketogenic diet and/or vagus nerve stimulation.

Guidelines/Recommendations
The American Academy of Neurology and the American Epilepsy Society published a guideline update for treatment-resistant epilepsy (2018) stating that clobazam is probably effective as add-on therapy for LGS and is possibly effective as add-on therapy for treatment-resistant adult focal epilepsy.[13] Adjunctive therapy with clobazam has been effective in the treatment of uncontrolled or refractory epilepsy in adults and children.[14] If first-line treatment is ineffective or not tolerated, clobazam has been used as adjunctive treatment of refractory focal seizures (partial seizure and localization-related seizure) in children, young adults, and adults; adjunctive treatment of generalized tonic-clonic seizures in children, young adults, and adults; and adjunctive treatment of children and young adults with benign epilepsy with centrotemporal spikes, Panayiotopoulos syndrome or late-onset childhood occipital epilepsy (Gastaut type).

Lennox-Gastaut Syndrome
Currently, the FDA-approved drugs for this condition are Epidiolex® (cannabidiol oral solution), felbamate, lamotrigine, rufinamide tablets and oral suspension, topiramate, clobazam, and Fintepla® (fenfluramine oral solution).[11,14] Despite the lack of level I or level II evidence, valproic acid remains a mainstay in treatment.[5,6,12] If valproic acid does not provide adequate seizure control, which is almost always the case, lamotrigine should be added as the first adjunctive therapy.[4] If the combination regimen of valproic acid and lamotrigine does not provide adequate control, then rufinamide should be initiated and either valproic acid or lamotrigine should be discontinued. If seizure control is still not achieved, the next adjunctive therapies to consider are topiramate, clobazam, and felbamate. There is limited evidence for the use of levetiracetam, zonisamide, and Fycompa® (perampanel tablet, oral suspension). Where possible, no more than two ASMs should be used concomitantly; use of multiple ASMs raises the risk of adverse effects and/or drug-drug interactions.

Dravet Syndrome
Valproic acid and clobazam are considered to be the first-line treatment for Dravet syndrome.[7,9,10] If seizure control is suboptimal, Diacomit® (stiripentol capsules), Epidiolex, Fintepla, and topiramate are treatment options. If control is still inadequate, other therapies to consider are clonazepam, levetiracetam, and zonisamide. Drugs that should be avoided in Dravet syndrome include sodium channel blockers (e.g., carbamazepine, oxcarbazepine, lamotrigine, and phenytoin), Sabril® (vigabatrin tablet, oral packet), and tiagabine.

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