PRIOR AUTHORIZATION POLICY

POLICY: Antiseizure Medications – Clobazam Products Prior Authorization Policy
- Onfi® (clobazam tablets and oral suspension – Lundbeck, generic)
- Sympazan® (clobazam oral soluble film – Aquestive Therapeutics)

REVIEW DATE: 10/15/2025

INSTRUCTIONS FOR USE

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CIGNA NATIONAL FORMULARY COVERAGE:

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.[3-6] Affected children experience several different types of seizures, most commonly atonic seizures (sudden loss of muscle tone and limpness) and tonic seizures. 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). 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 20,000 to 40,000 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.[11] Adjunctive therapy with clobazam has been effective in the treatment of uncontrolled or refractory epilepsy in adults and children.[12] 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 (LGS)

Currently, the FDA-approved drugs for this condition are Fintepla® (fenfluramine oral solution), clobazam, clonazepam, rufinamide, Epidiolex® (cannabidiol oral solution), felbamate, lamotrigine, and topiramate.[5] To address the lack of treatment algorithm, the Lennox-Gastaut Syndrome Special Interest Group of the Pediatric Epilepsy Research Consortium (PERC) formed a core working group focused on ASM selection in this patient population (2025). Despite the lack of specific FDA labeling for LGS, valproic acid remains a mainstay in treatment.[5,6] Valproic acid is considered a first-line pharmacological therapy but should be avoided in women of childbearing potential due to potential teratogenic effects.[5] Clobazam is recommended as a first-line option, particularly for managing disabling drop seizures, while it may be considered a second-line option in other cases. Cannabidiol may be considered a second-line therapy, specifically when combined with clobazam; otherwise, it is generally listed as a third-line treatment. Lamotrigine is considered a second-line therapy when used alongside valproate to

enhance therapeutic synergy or in patients at risk of cognitive and behavioral side effects; otherwise, it can be utilized as a third- or fourth-line therapy depending on individual patient profiles. Rufinamide is a second-line option, particularly in cases where valproate or clobazam must be avoided, though it may be used as a third- or fourth-line option if these medications are tolerated. Topiramate can be considered from second- to fourth-line therapy, depending on the patient's cognitive profile, as well as the suitability and availability of other ASMs. Additional later-line options include levetiracetam, brivaracetam, Fycompa® (perampanel tablet, oral suspension), zonisamide, Fintepla, and felbamate. In managing LGS, monotherapy is rarely effective, which necessitates the use of combination therapy with two or three ASMs with varying mechanisms of action. However, where possible, no more than two ASMs should be used concomitantly; use of multiple ASMs raise the risk of side effects and/or drug-drug interactions. In addition to pharmacological options, non-pharmacological therapies offer significant benefits in managing LGS and include neuromodulation, resective surgery, corpus callosotomy, and the ketogenic diet.

Dravet Syndrome

At this time, there are three drugs approved for the treatment of seizures associated with Dravet syndrome: Diacomit® (stiripentol capsules, powder for oral suspension), Epidiolex, and Fintepla.[12] An expert panel considers valproic acid to be the first-line treatment for Dravet syndrome.[9] Clobazam, Diacomit, and Fintepla can be considered as either first- or second-line ASMs. Cannabidiol was supported either as first- or second-line treatment. There was modest consensus among caregivers, but no consensus among physicians to support topiramate as first-, second-, or third-line therapy. The Dravet Foundation states that Diacomit, Epidiolex, and Fintepla are considered first-line agents for the treatment of Dravet syndrome.[7] If control is still inadequate, other therapies to consider are clonazepam, levetiracetam, and zonisamide.[7,9] Sodium channel blockers (e.g., carbamazepine, oxcarbazepine, lamotrigine, and phenytoin) can worsen seizures in Dravet syndrome. Additionally, vigabatrin and tiagabine may increase the frequency of myoclonic seizures and should be avoided.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of clobazam. Because of the specialized skills required for evaluation and diagnosis of patients treated with clobazam as well as the monitoring required for adverse events and long-term efficacy, initial approval requires clobazam to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the duration noted below.

- **Onfi® (clobazam tablets and oral suspension – Lundbeck, generic) Sympazan® (clobazam oral soluble film – Aquestive Therapeutics) is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):**

FDA-Approved Indication

1. **Lennox-Gastaut Syndrome.** Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient is ≥ 2 years of age; AND
     - **ii.** Patient has tried and/or is concomitantly receiving ONE of the following (a or b):
       - **a)** At least two other antiseizure medications; OR
         Note: Examples of other antiseizure medications include valproic acid, levetiracetam, zonisamide, Fycompa (perampanel tablet or oral suspension), vigabatrin, others.
       - **b)** One of lamotrigine, topiramate, rufinamide, felbamate, Fintepla (fenfluramine oral solution), or Epidiolex (cannabidiol oral solution); AND
     - **iii.** The medication is prescribed by or in consultation with a neurologist; OR
   - **B)** Patient is Currently Receiving Clobazam. Approve if the patient is responding to therapy, as determined by the prescriber.
     Note: Examples of therapy response include reduced seizure severity, frequency, and/or duration from baseline (prior to initiation of clobazam).

Other Uses with Supportive Evidence

2. **Dravet Syndrome.** Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets BOTH of the following (i and ii):
     - **i.** Patient is ≥ 2 years of age; AND
     - **ii.** The medication is prescribed by or in consultation with a neurologist; OR
   - **B)** Patient is Currently Receiving Clobazam. Approve if the patient is responding to therapy, as determined by the prescriber.
     Note: Examples of therapy response include reduced seizure severity, frequency, and/or duration from baseline (prior to initiation of clobazam).

3. **Treatment-Refractory Seizures/Epilepsy.** Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient is ≥ 2 years of age; AND
     - **ii.** Patient has tried and/or is concomitantly receiving at least two other antiseizure medications; AND
       Note: Examples of other antiseizure medications are valproic acid, lamotrigine, topiramate, clonazepam, levetiracetam, zonisamide, rufinamide, felbamate.
     - **iii.** The medication is prescribed by or in consultation with a neurologist; OR
   - **B)** Patient is Currently Receiving Clobazam. Approve if the patient is responding to therapy, as determined by the prescriber.

Note: Examples of therapy response include reduced seizure severity, frequency, and/or duration from baseline (prior to initiation of clobazam).

CONDITIONS NOT COVERED

- **Onfi® (clobazam tablets and oral suspension – Lundbeck, generic) Sympazan® (clobazam oral soluble film – Aquestive Therapeutics) is(are) considered not medically necessary for ANY other use(s); criteria will be updated as new published data are available.**

REFERENCES

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	The policy name was changed from Antiepileptics – Clobazam Prior Authorization Policy to Antiseizure Medications – Clobazam Prior Authorization Policy. Throughout the criteria, reference to antiepileptic medications was changed to antiseizure medications. **Lennox-Gastaut Syndrome:** The addition of Fintepla to the list of "one of the following" antiseizure medications that a patient has tried and/or is concomitantly receiving. Examples of other antiseizure medications were moved to a Note.	11/15/2023
Annual Revision	No criteria changes.	11/13/2024

Annual Revision	No criteria changes.	10/15/2025