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: 11/13/2024

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 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.[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).

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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.

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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of clobazam is recommended in those who meet one of the following criteria:

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), vigabatrin, others.
       - **b)** One of lamotrigine, topiramate, rufinamide, felbamate, Fintepla (fenfluramine oral solution), or Epidiolex (cannabidiol oral solution); AND
     - **iii.** Clobazam is prescribed by or in consultation with a neurologist.
   - **B)** Patient is Currently Receiving Clobazam. Approve if the patient is responding to therapy, as determined by the prescriber.

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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.** Clobazam is prescribed by or in consultation with a neurologist.
   - **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.** Clobazam is prescribed by or in consultation with a neurologist.
   - **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 RECOMMENDED FOR APPROVAL

Coverage of clobazam is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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