Oscar Clinical Guideline: Epidiolex (cannabidiol) (PG050, Ver. 5)

# Epidiolex (cannabidiol)

**Disclaimer**

*Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.*

*Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.*

## Summary

Lennox-Gastaut syndrome is a severe developmental epileptic encephalopathy with multiple etiologies. This disorder is characterized by several seizure types, often resistant to treatment, and severe cognitive impairment. Seizures typically begin before the age of 8 years and persist into adulthood. Multiple medications are approved for the treatment of Lennox-Gastaut syndrome, with clobazam and valproic acid typically being considered first-line agents. However, it should be noted that treatment must be individualized based on the patient's response and tolerance to these medications.

Dravet syndrome is a severe, lifelong form of epilepsy that begins in the first year of life with frequent or prolonged seizures often triggered by fever or hot weather. Treatments for Dravet syndrome aim to manage seizure frequency and length. Similar to Lennox-Gastaut syndrome, clobazam and valproic acid are often considered first-line agents, but the selection of treatment should be tailored to individual patient needs.

Tuberous sclerosis complex (TSC) is a genetic disorder that causes non-cancerous (benign) tumors to grow in many parts of the body. It is often detected during infancy or childhood, commonly affecting the brain, eyes, kidneys, heart, lungs, and skin. Seizures, known as infantile spasms, are often the first sign of TSC. Despite the tumors associated with TSC often being benign, patients are at an increased risk for developing malignant tumors during their lifetime. Management of TSC focuses on symptomatic treatment, which often includes antiepileptic medications for seizure control.

Cannabidiol (Epidiolex) is an FDA-approved medication for the treatment of seizures associated with Lennox-Gastaut Syndrome, Dravet Syndrome, and Tuberous Sclerosis Complex, particularly in patients who have not responded adequately to other antiepileptic medications. Studies have demonstrated that Epidiolex can significantly reduce the incidence of seizures in these conditions. It is important to note that Epidiolex can cause elevated liver enzymes, therefore liver function tests (ALT, AST) and total bilirubin baseline levels should be assessed before initiation of treatment. Epidiolex is administered as an oral solution twice daily, usually in combination with other antiepileptic medications.

**Table 1: Epidiolex (cannabidiol) Dosage Information**

| Indication | Initial dose | Maximum dose | Additional Considerations |
|---|---|---|---|
| Lennox-Gastaut Syndrome | 2.5 mg/kg twice daily - may increase dosage each week by 5mg/kg/day | 10 mg/kg twice daily = total 20mg/kg/day | Requires dose titration when starting or stopping therapy |
| Dravet Syndrome | 2.5 mg/kg twice daily - may increase dosage each week by 5mg/kg/day | 10 mg/kg twice daily = total 20mg/kg/day | Requires dose titration when starting or stopping therapy |
| Tuberous Sclerosis Complex | 2.5 mg/kg twice daily - may increase dosage each week by 5mg/kg/day | 12.5 mg/kg twice daily = total 25mg/kg/day | Requires dose titration when starting or stopping therapy |

## Definitions

"**Antiepileptic drugs**" are medications used to control seizures. They work in different ways to reduce the excess electrical activity in the brain that leads to seizures.

"**Bilirubin**" is a substance made during the normal breakdown of red blood cells. Bilirubin passes through the liver and is eventually excreted out of the body. Higher than normal levels of bilirubin may indicate different types of liver problems.

"**Cognitive impairment**" refers to problems with cognitive functions such as thinking, learning, memory, and problem-solving. Cognitive impairments range in severity from mild to severe, and they are a common feature of many neurological conditions.

"**Epileptic encephalopathy**" is a severe brain disorder identified at an early age in which seizures cause severe cognitive and behavioral impairments.

"**First-line agents**" refer to the initial or preferred medication or treatment typically used because it is effective and has acceptable side effects.

"**Seizure**" is a sudden, uncontrolled electrical disturbance in the brain. It can cause changes in behavior, movements or feelings, and in levels of consciousness. There are several types of seizures, which range in severity.

"**Serum transaminases**" consist of Alanine transaminase (ALT) and Aspartate transaminase (AST) and are enzymes found in the liver that help convert proteins into energy for the liver cells. When the liver is damaged, ALT and/or AST are released into the bloodstream and levels increase.

## Medical Necessity Criteria for Initial Authorization

The Plan considers **cannabidiol (Epidiolex)** medically necessary when **ALL** the following criteria are met:

1. The medication is being prescribed by a neurologist or a healthcare provider with expertise in managing epilepsy**; *AND***
2. The member is at least 1 year old**; *AND***
3. The medication is being prescribed for the treatment of seizures associated with **ONE** of the following:
    a. Dravet syndrome (DS)**; *or***
    b. Lennox-Gastaut syndrome (LGS)**; *or***
    c. Tuberous Sclerosis Complex (TSC)**; *AND***
4. The member is unable to use, or has adequately tried and failed at least **TWO** generic antiepileptic drugs for at least a 1 month duration (i.e valproic acid, lamotrigine, topiramate, levetiracetam, felbamate, and clobazam)**; *AND***

5. The member has documentation of serum transaminases (ALT and AST) and total bilirubin baseline levels prior to initiating therapy**; *AND***
6. Epidiolex (cannabidiol) is being prescribed within the manufacturer's published dosing guidelines or falls within dosing guidelines found in a compendia of current literature:
    a. For LGS and DS indications, maximum daily dose = 20mg/kg/day**; *or***
    b. For TSS indication, maximum daily dose = 25mg/kg/day**; *AND***
7. Chart documentation and supporting lab work (e.g., ALT, AST, and total bilirubin) are provided for review to substantiate the above listed requirements.

**If the above prior authorization criteria are met, cannabidiol (Epidiolex) will be approved for 6 months.**

## Medical Necessity Criteria for Reauthorization

Reauthorization for 12 months will be granted if **BOTH** of the following are met:

1. The member still meets the applicable initial criteria; ***AND***
2. Chart documentation shows the member has experienced a clinical improvement in symptoms since starting the requested medication as evidenced by **ONE** of the following:
    a. A reduction in the severity of seizures***; and/or***
    b. A reduction in the frequency of seizures.

## Experimental or Investigational / Not Medically Necessary

Cannabidiol (Epidiolex) for any other indication is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven.

## References


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4. Lattanzi S, Trinka E, Striano P et al. Highly Purified Cannabidiol for Epilepsy Treatment: A Systematic Review of Epileptic Conditions Beyond Dravet Syndrome and Lennox-Gastaut Syndrome. CNS Drugs. 2021; 35:265-281.
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## Clinical Guideline Revision / History Information

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