PRIOR AUTHORIZATION POLICY

POLICY: Antiseizure Medications – Epidiolex Prior Authorization Policy
- Epidiolex® (cannabidiol oral solution – Jazz)

REVIEW DATE: 02/11/2026

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. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. 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.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Epidiolex, a cannabinoid, is indicated in patients ≥ 1 year of age for the **treatment of seizures associated with**:[1]
- **Dravet syndrome**.
- **Lennox-Gastaut syndrome**.
- **Tuberous sclerosis complex**.

Disease Overview

Dravet syndrome is a rare genetic epileptic encephalopathy marked with frequent and/or prolonged seizures.[2,3] 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.[3] Two or more antiseizure medications (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, reduction in overall seizure frequency, and minimization of treatment side effects.[4,5]

Lennox-Gastaut syndrome, a severe epileptic and developmental encephalopathy, is associated with a high rate of morbidity and mortality.[6,7] Lennox-Gastaut syndrome most often begins between 3 and 5 years of age.[6-9] Affected children experience several different types of seizures, most commonly atonic seizures (sudden loss of muscle tone and limpness) and tonic seizures.[6,9] The three main forms of treatment of Lennox-Gastaut syndrome are ASMs, dietary therapy (typically the ketogenic diet), and device/surgery (e.g., vagus nerve stimulation, corpus callostomy).[9] None of the therapies are effective in all cases of Lennox-Gastaut syndrome and the disorder has proven particularly resistant to most therapeutic options.

Tuberous sclerosis complex is a rare, genetic disease that causes non-cancerous (benign) tumors to grow in the brain and on other vital organs such as the kidneys, heart, eyes, lungs, and skin.[10] It can result in a combination of symptoms including seizures, impaired intellectual development, autism, behavioral problems, skin abnormalities, and kidney disease. Seizures affect most individuals with tuberous sclerosis complex at some point during their life and can be difficult to control.

Clinical Efficacy in Other Refractory Seizures

In 2014, an expanded access program was initiated to provide Epidiolex to patients with treatment-resistant epilepsy.[11] Of the 840 patients included in a published review, 192 patients were diagnosed with Dravet syndrome or Lennox-Gastaut syndrome, and 648 patients were diagnosed with other conditions, including CDKL5 deficiency disorder; Dup15q, Aicardi, and Doose syndromes; febrile infection-related epilepsy syndromes; focal epilepsy; tuberous sclerosis complex; Sturge-Weber syndrome; lissencephaly; cortical malformation/dysplasia; and myoclonic absence. The patients enrolled in the study had severe, intractable, childhood-onset treatment-resistant epilepsy and were on stable doses of ASMs for 4 weeks before starting Epidiolex as add-on therapy. Reduced seizure frequency was observed across the expanded access program and in additional cohort analyses.[11-13]

Guidelines/Recommendations

Dravet Syndrome

At this time, there are three drugs approved for the treatment of seizures associated with Dravet syndrome: Epidiolex, Diacomit® (stiripentol capsules, powder for oral suspension), and Fintepla® (fenfluramine oral solution).[1,14,15] An international consensus on diagnosis and management of Dravet syndrome was published in 2022; physician and caregiver perspectives were considered.[16] There was strong consensus that valproic acid is an appropriate first-line ASM and clobazam can be considered either first- or second-line. Additional consensus for the first-line setting among physicians included Fintepla (strong) and Diacomit (moderate). Physicians did not reach consensus regarding the use of Epidiolex as either first- or second-line treatment. It was noted with moderate consensus that lamotrigine is contraindicated in Dravet syndrome.

The Dravet Foundation states that Diacomit, Epidiolex, and Fintepla are considered first-line agents for the treatment of Dravet syndrome.[2] If control is still inadequate,

other therapies to consider are clonazepam, levetiracetam, and zonisamide.[2,4] 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.

Lennox-Gastaut Syndrome
Currently, the FDA-approved drugs for this condition are Fintepla, clobazam, clonazepam, rufinamide (Banzel®, generic), Epidiolex, felbamate, lamotrigine, and topiramate.[17] To address the lack of treatment algorithm, the Lennox-Gastaut syndrome Special Interest Group of the Pediatric Epilepsy Research Consortium formed a core working group focused on ASM selection in this patient population (2025). Despite the lack of specific FDA labeling for Lennox-Gastaut syndrome, valproic acid remains a mainstay in treatment.[9,17] Valproic acid is considered a first-line pharmacologic therapy but should be avoided in women of childbearing potential due to potential teratogenic effects.[17] 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. Epidiolex may be considered a second-line therapy, specifically when combined with clobazam; otherwise, it is generally listed as a third-line treatment. Many other options are cited in the second- or later-line settings including lamotrigine, rufinamide, topiramate, levetiracetam, brivaracetam, perampanel (Fycompa®, generic), zonisamide, Fintepla, and felbamate; refer to the consensus algorithm for additional detail. Monotherapy is rarely effective in managing Lennox-Gastaut syndrome, 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.

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

- **Epidiolex® (cannabidiol oral solution – Jazz)**

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 Indications

1. **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 ALL of the following (i, ii, and iii):
      i. Patient is ≥ 1 year of age; AND
      ii. Patient meets ONE of the following (a or b):
         a) Patient has tried or is concomitantly receiving at least two other antiseizure medications; OR
         Note: Examples of other antiseizure medications include valproic acid, topiramate, clonazepam, levetiracetam, zonisamide.
         b) Patient has tried or is concomitantly receiving one of Fintepla (fenfluramine oral solution), Diacomit (stiripentol capsules, powder for oral suspension), or clobazam; AND
      iii. The medication is prescribed by or in consultation with a neurologist; OR
   B) Patient is Currently Receiving Epidiolex. Approve if the patient is responding to therapy (e.g., reduced seizure severity, frequency, and/or duration) as determined by the prescriber.

2. **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 ≥ 1 year of age; AND
      ii. Patient has tried or is concomitantly receiving at least two other antiseizure medications; AND
      Note: Examples of other antiseizure medications include lamotrigine, topiramate, rufinamide, felbamate, clobazam, valproic acid, levetiracetam, zonisamide, perampanel, vigabatrin.
      iii. The medication is prescribed by or in consultation with a neurologist; OR
   B) Patient is Currently Receiving Epidiolex. Approve if the patient is responding to therapy (e.g., reduced seizure severity, frequency, and/or duration) as determined by the prescriber.

3. **Tuberous Sclerosis Complex.** 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 ≥ 1 year of age; AND
      ii. Patient has tried or is concomitantly receiving at least two other antiseizure medications; AND

Note: Examples of other antiseizure medications include valproic acid, lamotrigine, topiramate, clonazepam, levetiracetam, zonisamide, rufinamide, felbamate, clobazam, perampanel, vigabatrin, everolimus.

iii. The medication is prescribed by or in consultation with a neurologist; OR

B) Patient is Currently Receiving Epidiolex. Approve if the patient is responding to therapy (e.g., reduced seizure severity, frequency, and/or duration) as determined by the prescriber.

Other Uses with Supportive Evidence

4. **Treatment-Refractory Seizures/Epilepsy (Specific Rare Conditions)**. Approve for 1 year if the patient meets ONE of the following (A or B):
   Note: The specific rare conditions which fall under this approval condition are CDKL5 deficiency disorder; Dup15q, Aicardi, or Doose syndromes; febrile infection-related epilepsy syndromes; focal epilepsy; Sturge-Weber syndrome; lissencephaly; cortical malformation/dysplasia; and epilepsy with myoclonic absences.
   A) Initial Therapy. Approve if the patient meets ALL of the following (i, ii, and iii):
      i. Patient is ≥ 1 year of age; AND
      ii. Patient has tried or is concomitantly receiving at least two other antiseizure medications; AND
      Note: Examples of other antiseizure medications include valproic acid, lamotrigine, topiramate, clonazepam, levetiracetam, zonisamide, rufinamide, felbamate, clobazam, perampanel, vigabatrin.
      iii. The medication is prescribed by or in consultation with a neurologist; OR
   B) Patient is Currently Receiving Epidiolex. Approve if the patient is responding to therapy (e.g., reduced seizure severity, frequency, and/or duration) as determined by the prescriber.

CONDITIONS NOT COVERED

- **Epidiolex® (cannabidiol oral solution – Jazz)**

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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17. Samanta D, Bhalla S, Bhatia S, et al. Antiseizure medications for Lennox-Gastaut Syndrome: Comprehensive review and proposed consensus treatment algorithm. *Epilepsy Behav*. 2025;164:110261.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	02/07/2024
Annual Revision	**Treatment-Refractory Seizures/Epilepsy [specific rare conditions]:** The conditions covered were expanded to include focal epilepsy.	02/05/2025
Annual Revision	**Dravet Syndrome:** In the list of other antiseizure medications tried, the generic names for Fintepla (fenfluramine oral solution) and Diacomit (stiripentol capsules, powder for oral suspension) were added for clarity. **Lennox-Gastaut Syndrome:** Under examples of other antiseizure medications, Banzel was updated to rufinamide and Fycompa was updated to perampanel to reflect generic availability of these products. **Tuberous Sclerosis Complex:** Under examples of other antiseizure medications, Banzel was updated to rufinamide and Fycompa was updated to perampanel to reflect generic availability of these products. **Treatment-Refractory Seizures/Epilepsy (Specific Rare Conditions):** The specific rare conditions which fall under this approval condition were moved to a Note. Additionally, under examples of other antiseizure medications, Banzel was updated to rufinamide and Fycompa was updated to perampanel to reflect generic availability of these products.	02/11/2026