Pharmacy Policy Bulletin: J-0798 Epidiolex (cannabidiol oral solution) – Commercial and Healthcare Reform	
Number: J-0798	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0798-009	**Original Date:** 08/01/2018
Effective Date: 10/28/2024	**Review Date:** 10/02/2024

Drugs Product(s):	• Epidiolex (cannabidiol oral solution)
FDA-Approved Indication(s):	• Treatment of seizures in patients 1 year of age and older associated with: ○ Lennox-Gastaut syndrome (LGS) ○ Dravet syndrome (DS) ○ Tuberous sclerosis complex (TSC)

Background:	• Epidiolex is the only FDA-approved cannabidiol (CBD) oral solution. • Epidiolex is a plant-derived CBD that exhibits anticonvulsive effects. CBD does not appear to exert its anticonvulsant effects through interaction with cannabinoid receptors, and its exact mechanism is unknown. It is theorized that CBD may modulate neuronal inhibition, inhibit intracellular calcium release, and have anti-inflammatory effects. • Epidiolex is nearly 100% pure CBD, therefore, Epidiolex has no euphoric or intoxicating side effects typically associated with tetrahydrocannabinol (THC) derivatives. • LGS is a severe form of childhood epilepsy. It is characterized by cognitive dysfunction, multiple generalized seizure types, and a slow spike-wave electroencephalogram (EEG) pattern. • Multiple treatment modalities exist for LGS. While not FDA-approved, valproic acid is most often used first line. The American Academy of Neurology (AAN) guidelines currently recommend using rufinamide or clobazam as adjunctive therapies for LGS. The National Organization for Rare Disease (NORD) additionally recommends topiramate, lamotrigine, felbamate, rufinamide, clobazam and cannabidiol as adjunctive therapies. Due to serious side effects, felbamate is typically not used first or second line. • DS is a rare, drug-resistant epilepsy that typically appears in the first year of life in an otherwise healthy infant. It usually presents as a prolonged seizure that affects one side of the body and fever. • A 2022 international consensus on diagnosis and management of Dravet syndrome recommends valproate as first line therapy; fenfluramine, stiripentol, or

	clobazam as second line therapy; pharmaceutical grade cannabidiol as third line; and topiramate or ketogenic diet as fourth line. The following drugs should be avoided in Dravet syndrome: carbamazepine, oxcarbazepine, lamotrigine, and phenytoin. • TSC is a rare genetic disorder characterized by the growth of numerous benign tumors in many parts of the body. Some individuals with TSC have seizures or benign brain tumors that can cause serious or life-threatening complications. TSC affects approximately 1 in 6,000 newborns. • The international consensus statement on TSC states that anticonvulsant therapy for seizure types should generally follow that of other epilepsies. Other than for infantile spasms in TSC, there is little evidence to guide specific anticonvulsant treatment. • In clinical trials for Epidiolex, patients were inadequately controlled on at least one AED. • Prescribing Considerations: ○ The member should be under the supervision of a neurologist or pediatric and epilepsy specialist. ○ Due to risk of hepatocellular injury, obtain serum transaminases and total bilirubin levels in all patients prior to starting treatment. Concomitant use of high doses of Epidiolex and valproate increases the risk of transaminase elevations. ○ Epidiolex should be gradually withdrawn to minimize risk of increased seizure frequency and status epilepticus. ○ Clinical studies of Epidiolex excluded patients that used cannabis or synthetic cannabinoids within 90 days of the study and were unwilling to abstain during the study duration.

Approval Criteria

I. Initial Authorization

A. Lennox-Gastaut Syndrome

When a benefit, coverage of Epidiolex may be approved when all of the following criteria are met **(1. through 4.)**:

1. The member is 1 year of age or older.
2. The member has a diagnosis of Lennox-Gastaut syndrome (LGS) (ICD-10: G40.81).
3. Treatment is in combination with other conventional agents.
4. The member has experienced therapeutic failure, contraindication, or intolerance to at least two (2) plan-preferred generic products **(a. through d.)**:
   a. Valproic acid or divalproex sodium
   b. Topiramate
   c. Lamotrigine
   d. Clobazam

B. Dravet Syndrome

When a benefit, coverage of Epidiolex may be approved when all of the following criteria are met **(1. through 4.)**:

1. The member is 1 year of age or older.
2. The member has a diagnosis of Dravet syndrome (DS) (ICD-10: G40.83).
3. Treatment is in combination with other conventional agents.
4. The member has experienced therapeutic failure, contraindication, or intolerance to at least two (2) generic products **(a., b., or c.)**:
   a. Valproic acid or divalproex sodium
   b. Plan-preferred topiramate
   c. Clobazam

C. Tuberous Sclerosis Complex

When a benefit, coverage of Epidiolex may be approved when all of the following criteria are met **(1. and 2.):**

1. The member is 1 year of age or older.

2. The member has a diagnosis of tuberous sclerosis complex (TSC) (ICD-10: Q85.1).

II. Reauthorization

When a benefit, reauthorization of Epidiolex may be approved when the following criterion is met **(A.)**:

A. The prescriber attests that the member has experienced a reduction in seizure frequency from baseline.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Epidiolex [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; March 2024.
2. Jazz Pharmaceuticals. Our Medicines. https://www.jazzpharma.com/medicines/our-medicines/. Accessed September 9, 2024.
3. National Organization for Rare Disorders. Lennox-Gastaut Syndrome. Available at: https://rarediseases.org/rare-diseases/lennox-gastaut-syndrome/. Accessed September 9, 2024.
4. Kanner A, Ashman E, Gloss D, et al. Practice guideline update summary: Efficacy and tolerability of the new antiepileptic drugs II: Treatment-resistant epilepsy. *Neurology.* July 10, 2018;91(2).
5. National Organization for Rare Disorders. Dravet Syndrome. Available at: https://rarediseases.org/rare-diseases/dravet-syndrome-spectrum/. Accessed September 9, 2024.
6. Epilepsies Guidance and Management. National Institute for Health and Clinical Excellence (NICE). The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care. London (UK): NICE; 2012 Jan. (Clinical guideline; no. 137).
7. Wirrell EC, Laux L, Donner E, et al. Optimizing the diagnosis and management of Dravet syndrome: Recommendations from a North American consensus panel. *Pediatr Neurol*. 2017;68:18-34 e3.
8. U.S. National Library of Medicine. Tuberous sclerosis complex. Available at: https://ghr.nlm.nih.gov/condition/tuberous-sclerosis-complex#synonyms. Accessed September 9, 2024.

9. Krueger D, Northrup H. Tuberous Sclerosis Complex Surveillance and Management: Recommendations of the 2012 International Tuberous Sclerosis Complex Consensus Conference. *Pediatr Neurol.* 2013;49:255-265.
10. Wirrell E, Hood V, Knupp K, et al. International consensus on diagnosis and management of Dravet syndrome. *Epilepsia*. 2022;63:1761–1777.

Pharmacy policies do not constitute medical advice, nor are they intended to govern physicians' prescribing or the practice of medicine. They are intended to reflect the plan's coverage and reimbursement guidelines. Coverage may vary for individual members, based on the terms of the benefit contract.

The plan retains the right to review and update its pharmacy policy at its sole discretion. These guidelines are the proprietary information of the plan. Any sale, copying or dissemination of the pharmacy policies is prohibited; however, limited copying of pharmacy policies is permitted for individual use.