



## **EPIDIOLEX (cannabidiol)**

### **RATIONALE FOR INCLUSION IN PA PROGRAM**

#### **Background**

Epidiolex (cannabidiol) is used to treat seizures associated with Lennox-Gastaut syndrome, Dravet syndrome, or tuberous sclerosis complex in patients 1 year of age or older. The precise mechanisms by which Epidiolex exerts its anticonvulsant effect in humans are unknown (1).

#### **Regulatory Status**

FDA-approved indications: Epidiolex indicated for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS), or tuberous sclerosis complex (TSC) in patients 1 year of age and older (1).

Epidiolex causes dose-related elevations of liver transaminases (alanine aminotransferase [ALT] and/or aspartate aminotransferase [AST]). In clinical trials, serum transaminase elevations typically occurred in the first two months of treatment initiation; however, there were some cases observed up to 18 months after initiation of treatment, particularly in patients taking concomitant valproate. Resolution of transaminase elevations occurred with discontinuation of Epidiolex or reduction of Epidiolex and/or concomitant valproate in about two-thirds of the cases. In about one-third of the cases, transaminase elevations resolved during continued treatment with Epidiolex without dose reduction (1).

When discontinuing Epidiolex, the dose should be decreased gradually. As with all antiepileptic drugs, abrupt discontinuation should be avoided when possible, to minimize the risk of increased seizure frequency and status epilepticus (1).

There are only four agents approved by the U.S. Food and Drug Administration (FDA) for the treatment of LGS: felbamate, lamotrigine, topiramate, and rufinamide. Because LGS is often refractory to treatment, many patients require polypharmacy. Medication selection is based on safety, tolerability, and efficacy. Therefore, patients often require other treatment options, including anticonvulsant medications not approved for treatment of LGS: Onfi (clobazam), valproate / valproic acid and levetiracetam (2).

Most patients with DS require two or more drugs to achieve reasonable seizure control, and choice of drugs should be individualized based on considerations of efficacy as well as side effects,



**BlueCross  
BlueShield**

Federal Employee Program.

## **EPIDIOLEX (cannabidiol)**

tolerability, and access. Typically a stepwise approach is taken, using valproate as a first-line drug in most patients and then adding clobazam if seizures remain poorly controlled despite adequate valproate dosing and serum levels (3).

The safety and effectiveness of Epidiolex in pediatric patients 1 year of age and older have been established (1).

### **Summary**

Epidiolex is indicated for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS) or tuberous sclerosis complex (TSC) in patients 1 year of age and older. The precise mechanisms by which Epidiolex exerts its anticonvulsant effect in humans are unknown. Cannabidiol does not appear to exert its anticonvulsant effects through interaction with cannabinoid receptors. Epidiolex has been associated with dose-related elevations of liver transaminases (alanine aminotransferase [ALT] and/or aspartate aminotransferase [AST]) (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Epidiolex while maintaining optimal therapeutic outcomes.

### **References**

1. Epidiolex [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; March 2024.
2. Montouris G. Rational approach to treatment options for Lennox-Gastaut syndrome Epilepsia, 52(Suppl. 5):10–20, 2011.
3. 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.