Epidiolex

Description

Epidiolex (cannabidiol)

Background
Epidiolex (cannabidiol) is used to treat seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 years of age or older. The precise mechanisms by which Epidiolex exerts its anticonvulsant effect in humans are unknown (1).

Regulatory Status
FDA-approved indication: Epidiolex indicated for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS) in patients 2 years 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, 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 2 years of age and older have
been established (1).

**Related policies**

Diacomit, Sympazan

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**Policy**

This policy statement applies to clinical review performed for pre-service (Prior Approval,
Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Epidiolex may be considered medically necessary for patients 2 years and older for the
treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome and if the
conditions indicated below are met.

Epidiolex may be considered investigational in patients less than 2 years of age and for all
other indications.
Prior-Approval Requirements

Age 2 years of age or older

Diagnoses

Patient must have ONE of the following:

1. Seizures associated with Lennox-Gastaut syndrome (LGS)
2. Seizures associated with Dravet syndrome (DS)

AND ALL of the following
   a. Serum transaminases (ALT and AST) and total bilirubin levels must be obtained prior to starting therapy and monitored periodically throughout therapy
   b. Inadequate treatment response, intolerance, or contraindication to TWO of the following medications:
      a. Clobazam
      b. Valproate / Valproic acid (i.e. Depakote, Depacon)
      c. Lamotrigine
      d. Levetiracetam
      e. Banzal (rufinamide)
      f. Topiramate
      g. Felbamate
   c. Prescriber will not exceed the FDA labeled dose of 20mg/kg/day

Prior–Approval Renewal Requirements

Age 2 years of age or older

Diagnoses

Patient must have ONE of the following:

1. Seizures associated with Lennox-Gastaut syndrome (LGS)
2. Seizures associated with Dravet syndrome (DS)

AND ALL of the following:
a. Serum transaminases (ALT and AST) and total bilirubin levels are monitored periodically throughout therapy
b. Prescriber will not exceed the FDA labeled dose of 20mg/kg/day

### Policy Guidelines

#### Pre–PA Allowance

None

#### Prior–Approval Limits

<table>
<thead>
<tr>
<th>Quantity</th>
<th>Maximum daily dose of 20mg/kg/day</th>
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<tbody>
<tr>
<td>Duration</td>
<td>12 months</td>
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#### Prior–Approval Renewal Limits

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### Summary

Epidiolex indicated for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS) in patients 2 years 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.
**5.75.22**

**Section:** Prescription Drugs  
**Effective Date:** April 1, 2019  
**Subsection:** Neuromuscular Agents  
**Original Policy Date:** October 1, 2018  
**Subject:** Epidiolex  
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**References**


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**Policy History**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>September 2018</td>
<td>Addition to PA</td>
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<tr>
<td>March 2019</td>
<td>Annual review and reference update. Reworded background and summary and reworded max dose of 20 mg/kg/day requirement per SME</td>
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**Keywords**

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This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 15, 2019 and is effective on April 1, 2019.