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5.75.022

Section:	Prescription Drugs	**Effective Date:**	January 1, 2024
Subsection:	Neuromuscular Agents	**Original Policy Date:**	October 1, 2018
Subject:	Epidiolex	**Page:**	1 of 6

Last Review Date: December 8, 2023

Epidiolex

Description

Epidiolex (cannabidiol)

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, 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).

Related policies
Diacomit, Fintepla, Nayzilam, Valtoco

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** if the conditions indicated below are met.

Epidiolex may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 1 year of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Seizures associated with Lennox-Gastaut syndrome (LGS)
    a. Prescriber will not exceed the FDA labeled dose of 20mg/kg/day
2. Seizures associated with Dravet syndrome (DS)
    a. Prescriber will not exceed the FDA labeled dose of 20mg/kg/day
3. Seizures associated with tuberous sclerosis complex (TSC)
    a. Prescriber will not exceed the FDA labeled dose of 25mg/kg/day

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. Patient is on **TWO** concomitant anti-seizure medications **OR** has had an 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
    h. Stiripentol (Dravet syndrome **only**)

Prior–Approval *Renewal* Requirements

Age 1 year of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Seizures associated with Lennox-Gastaut syndrome (LGS)
    a. Prescriber will not exceed the FDA labeled dose of 20mg/kg/day

2. Seizures associated with Dravet syndrome (DS)
    a. Prescriber will not exceed the FDA labeled dose of 20mg/kg/day
3. Seizures associated with tuberous sclerosis complex (TSC)
    a. Prescriber will not exceed the FDA labeled dose of 25mg/kg/day

AND the following:

a. Serum transaminases (ALT and AST) and total bilirubin levels are monitored periodically throughout therapy

Policy Guidelines

Pre–PA Allowance

None

Prior–Approval Limits

Quantity

Diagnosis	Maximum daily dose
Lennox-Gastaut syndrome (LGS)	20 mg/kg/day
Dravet syndrome (DS)	
Tuberous sclerosis complex (TSC)	25 mg/kg/day

Duration 12 months

Prior–Approval *Renewal* Limits

Same as above

Rationale

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.; January 2023.
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.

Policy History

Date	Action
September 2018	Addition to PA
March 2019	Annual review and reference update. Reworded background and summary and reworded max dose of 20 mg/kg/day requirement per SME
June 2020	Annual review and reference update
August 2020	Addition of indication: seizures associated with tuberous sclerosis complex (TSC). Age requirement changed from 2 years of age and older to 1 year of age and older
September 2020	Annual review
December 2020	Annual review
March 2021	Annual review and reference update
March 2022	Annual review and reference update
April 2022	Added t/f option of stiripentol for Dravet syndrome only, and added the option for the patient to be on two concomitant anti-seizure medications to match Fintepla
December 2022	Annual review and reference update. Changed policy number to 5.75.022
March 2023	Annual review and reference update
December 2023	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 8, 2023 and is effective on January 1, 2024.