PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 11/15/2018
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EPIDIOLEX® (cannabidiol) oral solution

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Epidiolex (cannabidiol) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with Neurologist

  2. Individual is 1 years of age or older

  3. A confirmed diagnosis of **ONE** of the following:
     a. Seizures associated with Lennox-Gastaut syndrome (LGS)
     b. Seizures associated with Dravet syndrome (DS)
     c. Seizures associated with Tuberous Sclerosis Complex (TSC)

  4. Individual has failure, contraindication, or intolerance to **TWO** the following preferred step therapy agents:
     a. Valproate
     b. Clobazam
     c. Topiramate
     d. Levetiracetam
     e. Lamotrigine
     f. Vigabatrin
     g. Everolimus

  5. **ALL** of the following baseline tests have been completed before initiation of treatment:
     a. Serum transaminases (ALT and AST) and total bilirubin

  6. Not using any other cannabinoid, including medical marijuana

  7. There are **NO** contraindications.
     a. Contraindications include:
        i. Hypersensitivity to cannabidiol, sesame seed oil, or any of the ingredients in Epidiolex

  Initial approval duration: 2 months

- **Criteria for continuation of coverage (renewal request):** Epidiolex (cannabidiol) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation Neurologist

  2. Individual's condition has responded while on therapy
     a. Response is defined as:
        i. **For LGS**: Achieved and maintains a reduction in frequency of drop seizures (atonic, tonic, or tonic-clonic seizures)

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ii. **For DS**: Achieved and maintains a reduction in frequency of convulsive seizures (all countable atonic, tonic, clonic, and tonic-clonic seizures)
iii. **For TSC**: Achieved and maintains a reduction in frequency of TSC-associated seizures

3. Individual has been adherent with the medication

4. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Hepatocellular injury
        ii. Suicidal behavior and ideation
        iii. Hypersensitivity reaction

5. Not using any other cannabinoid, including medical marijuana

6. There are no significant interacting drugs

Renewal duration: 12 months

Description:

Epidiolex (cannabidiol) 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.

Cannabidiol, the active ingredient in Epidiolex, is a cannabinoid that naturally occurs in the *Cannabis sativa* L. plant. The precise mechanisms by which it exerts its anticonvulsant effect in humans are unknown. Cannabidiol does not appear to exert its anticonvulsant effects through interaction with cannabinoid receptors.

LGS, also known as Lennox syndrome, is a severe and difficult-to-treat form of childhood-onset epilepsy that most often appears between the second and sixth year of life. It is characterized by frequent seizures and can include different seizure types, such as, tonic, atonic, atypical absence, and myoclonic seizures. There may be periods of frequent seizures mixed with brief, relatively seizure-free periods. Most children with LGS experience some degree of impaired intellectual functioning or information processing, along with developmental delays and behavioral disturbances. Systematic review of randomized controlled trials conclude that no drug is highly effective, although valproic acid, lamotrigine, topiramate, rufinamide, felbamate, clobazam, and cannabidiol are possibly helpful.

DS, previously known as severe myoclonic epilepsy of infancy, is a rare early-onset epileptic encephalopathy characterized by refractory epilepsy and neurodevelopmental problems beginning in infancy. Patients present in the first year of life with a prolonged, often febrile, clonic seizure in the setting of normal cognitive and motor development prior to seizure onset. In most, febrile and afebrile seizures, including episodes of status epilepticus, recur repeatedly in the weeks to months after the initial event, and psychomotor impairment begins thereafter. Myoclonus, both epileptic and non-epileptic, occurs frequently. The majority of older children and young adults

with DS have motor system dysfunction, gait and postural abnormalities, and cognitive and behavioral impairment. DS seizures tend to be refractory to most anti-seizure drugs, and some patients derive benefit from a ketogenic diet and vagus nerve stimulation. The most commonly used anti-seizure drugs include valproate, clobazam, topiramate, levetiracetam, stirpentol, cannabidiol, and fenfluramine. Most patients require two or more agents to achieve reasonable seizure control. Valproate is considered a first-line agent for DS with clobazam added as a second agent if valproate does not control seizures despite adequate valproate dosing and serum levels. Topiramate is a broad spectrum antiseizure agent that is also used as added on therapy.

TSC is an inherited neurocutaneous disorder involving many organ systems, including developmental delay and multiple benign hamartomas of the brain, eyes, heart, lung, liver, kidney, and skin. The expression of the disease varies substantially; some may demonstrate only dermatologic features of the disease while others may develop more serious neurologic or systemic manifestations. Management is directed towards neurologic (e.g. seizures) and systemic manifestations. Children with TSC and infantile spasms may be controlled with vigabatrin or corticotropin injection gel. Children with TSC and focal seizures may be controlled with narrow spectrum anticonvusants such as oxcarbamazeoine or carbamazepine. Refractory or intractable epilepsy may be controlled with cannabidiol or everolimus. The clinical trial summarized in the product labeling studied the add-on use of Epidolex (cannabidiol) in patients with a diagnosis of TSC and seizure that were inadequately controlled with at least one anticonvulsant. The most commonly used agents were valproate, vigabatrin, levetiracetam, and clobazam.

Resources:

Epidiolex (cannabidiol) product information, revised by manufacturer Greenwich Biosciences Inc 07-2020, at DailyMed http://dailymed.nlm.nih.gov accessed September 27, 2020.

Wilfong A. Epilepsy syndromes in chilfren. In: UpToDate, Nordli DR, Dashe JF (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Accessed on September 27, 2020.

Andrade DM, Nascimento FA. Dravet syndrome: Management and prognosis. In: UpToDate, Nordli DR, Dashe JF (Ed), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Accessed on September 27, 2020.

Randle S. Tuberous sclerosis complex: Management and prognosis. In: UpToDate, Firth HV, Pappo AS, Patterson MC, Dashe JF (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Accessed on September 27, 2020.

Glaze DG. Management and prognosis of infantile spasms. In: UpToDate, Nordli DR, Dashe JF (Ed), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Accessed on September 27, 2020.