Original Effective Date: 08/2020
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Policy Number: C19326-A

Epidiolex (cannabidiol)

PRODUCTS AFFECTED

Epidiolex (cannabidiol)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This 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 Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Lennox-Gastaut Syndrome, Dravet Syndrome, Tuberous Sclerosis Complex

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. SEIZURES ASSOCIATED WITH LENNOX-GASTAUT SYNDROME, DRAVET SYNDROME OR TUBEROUS SCLEROSIS COMPLEX:
1. (a) Documented diagnosis of Lennox-Gastaut syndrome

MOLINA REVIEWER NOTE: Diagnostic criteria can include (i) Multiple seizure types, particularly tonic and atypical absence seizures, but also atonic and myoclonic seizures. Periods of nonconvulsive status epilepticus occur in most cases at some stage. (ii) A slow (less than 2.5 hertz) spike-wave pattern on the interictal electroencephalogram (EEG) that is generalized and usually has highest amplitude in the frontal region (also called an "atypical spike and wave" pattern) or (iii) Mental retardation (occasionally progressive) with or without other neurologic abnormalities.

OR

(b) Documented diagnosis of Dravet syndrome

MOLINA REVIEWER NOTE: Based on the International League Against Epilepsy (ILAE) classification system diagnostic criteria can include (i) A family history of epilepsy or febrile convulsions, (ii) Normal development before onset of seizures, (iii) Seizures beginning before one year of age, (iv) Pleomorphic epilepsy (myoclonic, focal clonic, absence, and generalized seizures), (v) EEG with generalized spike waves and polyspike waves, (vi) Early photosensitivity or focal abnormalities, (vii) Psychomotor retardation after two years of age, (viii) Appearance of subsequent ataxia, pyramidal signs, or interictal myoclonus after the onset of psychomotor slowing or (ix) Exacerbation of seizures by hyperthermia

OR

(c) Documented diagnosis of tuberous sclerosis complex

AND

i. Documentation of TSC1 or TSC2 pathogenic mutation in DNA from normal tissue based on genetic testing

OR

ii. Documentation of clinical diagnostic criteria including two major clinical features OR one major and ≥ 2 minor clinical features

[Major clinical features: Hypomelanotic macules (≥3, at least 5 mm diameter), Angiofibromas (≥3) or fibrous cephalic plaque, Ungual fibromas (≥2), Shagreen patch (connective tissue nevus), Multiple retinal hamartomas, Cortical dysplasias (includes tubers and cerebral white matter radial migration lines), Subependymal nodules, Subependymal giant cell astrocytoma, Cardiac rhabdomyoma, Lymphangioleiomyomatosis (LAM), Angiomyolipomas (≥2)

Minor clinical features: "Confetti" skin lesions (1 to 2 mm hypomelanotic macules), Dental enamel pits (≥3), Intraoral fibromas (≥2), Retinal achromic patch, Multiple renal cysts, Nonrenal hamartomas]

AND

2. Documentation that seizures have been inadequately controlled by a trial of at least 2 antiepileptic drugs (e.g., clobazam, valproate, lamotrigine, levetiracetam, topiramate, felbamate) or have a labeled contraindication to clobazam, valproate, lamotrigine, levetiracetam, topiramate, and felbamate.

AND

3. Member continues treatment with at least one other antiepileptic drug (e.g., clobazam, valproate, lamotrigine, levetiracetam, vigabatrin, carbamazepine)

AND

4. Prescriber attests that serum transaminases and total bilirubin levels will be obtained prior to initiation, and 1 month, 3 months, and 6 months after initiation of treatment with Epidiolex, and periodically thereafter or as clinically indicated

AND

5. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Epidiolex (cannabidiol) include: Hypersensitivity to cannabidiol or any of the ingredients in Epidiolex.]

CONTINUATION OF THERAPY:

A. SEIZURES ASSOCIATED WITH LENNOX-GASTAUT SYNDROME, DRAVET SYNDROME OR

TUBEROUS SCLEROSIS COMPLEX:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
   AND
3. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms (e.g., reduced seizure activity, frequency, and/or duration)
   AND
4. Documentation that the member does not have sustained transaminase elevations greater than 5 times the upper limit of normal (5x ULN)
   AND
5. Documentation of continued medical need for the medication

DURATION OF APPROVAL:
Initial authorization: 12 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a neurologist or physician who specializes in the treatment of Lennox-Gastaut Syndrome, Dravet syndrome or tuberous sclerosis complex [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
1 year of age and older

QUANTITY:
Seizure associated with Lennox-Gastaut syndrome or Dravet syndrome: Maximum recommended dosage of 20 mg/kg/day
Seizure associated with tuberous sclerosis complex: Maximum recommended dose of 25mg/kg/day

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Anticonvulsants - Misc.

FDA-APPROVED USES:
Indicated for the treatment of seizures associated with Lennox-Gastaut syndrome, Dravet syndrome, or tuberous sclerosis complex in patients 1 year of age and older

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Dravet syndrome is a rare genetic condition that appears during the first year of life with frequent fever related seizures (febrile seizures). Later, other types of seizures typically arise, including myoclonic seizures (involuntary muscle spasms). Additionally, status epilepticus, a potentially life-threatening state of continuous seizure activity requiring emergency medical care, may occur. Children with Dravet syndrome typically experience poor development of language and motor skills, hyperactivity and difficulty relating to others.

Lennox-Gastaut syndrome begins in childhood. It is characterized by multiple types of seizures. People with Lennox-Gastaut syndrome begin having frequent seizures in early childhood, usually between ages 3 and 5. More than three-quarters of affected individuals have tonic seizures, which cause the muscles to contract uncontrollably. Almost all children with Lennox-Gastaut syndrome develop learning problems and intellectual disability. Many also have delayed development of motor skills, such as sitting and crawling. Most people with Lennox-Gastaut syndrome require help with usual activities of daily living.

Most children with epilepsy achieve reasonably good seizure control with antiseizure drug therapy, but some are refractory despite numerous medications. Medical treatment failure is often apparent early in the course of treatment. Children who fail to respond to antiseizure drug monotherapy at adequate doses or do not tolerate effective doses should be started on a second antiseizure drug, although the likelihood of complete seizure remission decreases with each subsequent failed antiseizure drug trial. Both LGS and Dravets have higher mortality rate than other types of epilepsy. The first antiseizure drug fails in 20 to 40 percent of children with epilepsy; lack of efficacy and side effects contribute roughly equally to treatment failure. Adding a second antiseizure drug is a reasonable next step when seizures are resistant to adequate doses of the initial drug

EPIDIOLEX is indicated for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 years of age and older.
Epidiolex is the first FDA-approved drug that contains a purified drug substance derived from marijuana. It is also the first FDA approval of a drug for the treatment of patients with Dravet syndrome. CBD is a chemical component of the Cannabis sativa plant, more commonly known as marijuana. However, CBD does not cause intoxication or euphoria (the “high”) that comes from tetrahydrocannabinol (THC). THC (and not CBD) that is the primary psychoactive component of marijuana.

EPIDIOLEX is to be administered orally with recommended starting dose of 2.5 mg/kg taken twice daily (5 mg/kg/day). After one week, the dosage can be increased to a maintenance dose of 5 mg/kg twice daily (10 mg/kg/day). Based on clinical response and tolerability, EPIDIOLEX can be increased up to a maximum recommended maintenance dosage of 10 mg/kg twice daily (20 mg/kg/day). Dosage adjustment is recommended for patients with moderate or severe hepatic impairment. Clinical trials have shown a reduction in seizure events of up to 40 percent across both indications.
Tuberous Sclerosis Complex (TSC) is a rare genetic disorder that causes benign tumors in many parts of the body. It is often detected during infancy or childhood. The disease can affect many different parts of the body. Growth in the brain can cause seizures, which is often the first observable symptom. Current indicated treatment options are limited.

In a double-blind, placebo-controlled randomized clinical trial (GWPCARE6) published in JAMA

Neurology December of 2020, investigators enrolled 224 patients with tuberous sclerosis complex. These patients were treated with cannabidiol (25 or 50 mg/kg/day) or matched placebo for 16 weeks and were currently taking at least 1 antiepileptic medication. The percentage reduction from baseline in the type of seizures considered the primary end point was 48.6% (95% CI, 40.4%-55.8%) for the CBD25group, 47.5% (95% CI, 39.0%-54.8%) for the CBD50 group, and 26.5% (95% CI, 14.9%-36.5%) for the placebo group; the percentage reduction from placebo was 30.1% (95% CI, 13.9%-43.3%; P < .001) for the CBD25 group and 28.5% (95% CI, 11.9%-42.0%; nominal P = .002) for the CBD50 group. The most common adverse events were diarrhea (placebo group, 19 [25%]; CBD25 group, 23 [31%]; CBD50 group, 41 [56%]) and somnolence (placebo group, 7 [9%]; CBD25 group, 10 [13%]; CBD50 group, 19 [26%]), which occurred more frequently with cannabidiol than placebo. Eight patients in CBD25 group, 10 in CBD50 group, and 2 in the placebo group discontinued treatment because of adverse events. Twenty-eight patients taking cannabidiol (18.9%) had elevated liver transaminase levels vs none taking placebo. Cannabidiol significantly reduced TSC-associated seizures compared with placebo. The 25-mg/kg/day dosage had a better safety profile than the 50-mg/kg/day dosage.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Epidiolex (cannabidiol) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Epidiolex (cannabidiol) include: Hypersensitivity to cannabidiol or any of the ingredients in Epidiolex.

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Epidiolex SOLN 100MG/ML (60 mL bottle, 100mL bottle)

REFERENCES

1. Epidiolex [package insert]. Carlsbad, CA: Greenwich Biosciences, Inc.; March 2024.
2. National Institute for Health and Care Excellence (2012). Epilepsies: diagnosis and management. NICE Guideline [CG137]. Updated April 2018. Available at: https://www.nice.org.uk/guidance/cg137. Accessed December 7, 2018.
3. Wirrell EC, Laux L, Donner E, et al. Optimizing the Diagnosis and Management of Dravet Syndrome: Recommendations From a North American Consensus Panel. Pediatric Neurology68 (2017) 18-34.
4. Devinsky O, Cross H, Laux L, et al. Trial of Cannabidiol for Drug-Resistant Seizures in the Dravet Syndrome. N Engl J Med 2017;376:2011-20.
5. Thiele EA, Marsh ED, French JA, et al. Cannabidiol in patients with seizures associated with Lennox-Gastaut syndrome (GWPCARE4): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet;391:1085-96, Published online January 24, 2018. Available at:

http://dx.doi.org/10.1016/S0140-6736(18)30136-3
6. Thiele, E. A., Bebin, E. M., Bhathal, H., Jansen, F. E., Kotulska, K., Lawson, J. A., O'Callaghan, F. J., Wong, M., Sahebkar, F., Checketts, D., Knappertz, V., & GWPCARE6 Study Group (2020). Add-On Cannabidiol Treatment for Drug-Resistant Seizures in Tuberous Sclerosis Complex: A Placebo-Controlled Randomized Clinical Trial. JAMA neurology, e204607. Advance online publication. https://doi.org/10.1001/jamaneurol.2020.4607
7. Epilepsy Foundation. LGS: Seizure Medications. Available at: https://www.epilepsy.com/learn/types-epilepsy-syndromes/lennox-gastaut- syndrome-lgs/treatment/lgs-seizure-medications. Accessed January 22, 2019.

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Quantity References	Q2 2024
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Duration of Approval References	Q2 2023
REVISION- Notable revisions: Required Medical Information Continuation of Therapy	Q2 2022
Q2 2022 Established tracking in new format	Historical changes on file