PRACTICE AID

FDA-Approved Cannabidiol (CBD; Epidiolex) Patient Information Guide[1-4]

Full abbreviations, accreditation, and disclosure information available at **PeerView.com/Epilepsy2020**

PeerView INSTITUTE FOR MEDICAL EDUCATION

MLI Medical Learning Institute, Inc.

What Is CBD (Epidiolex)?

- First and only FDA-approved prescription CBD oral solution to treat seizures associated with LGS, DS, or TSC in patients >1 year of age
- Active ingredient is a highly purified form of CBD that comes from the cannabis plant

How Does the FDA-Approved Rx CBD (Epidiolex) Differ From Non-Rx Dispensary or Online CBD Products?

Non-Rx Dispensary and Online CBD	FDA-Approved Rx CBD (Epidiolex)
GROWING CONDITIONS	
• Cannabis plants absorb chemicals and toxins from soil • Light/dark cycle affects expression of cannabinoids • Non-Rx CBD is grown in unknown conditions	Each cannabis plant is • Grown in its own container with controlled light, water, and soil • Guaranteed to have no pesticides, heavy metals, mold or yeast, or genetic modifications
CONSISTENCY	
• For medical treatment, it's important to keep a consistent dose from batch to batch • The actual content of THC and/or CBD used in dispensary products may be uncertain or unreliable	• Every bottle of Rx CBD (Epidiolex) has exact ingredients listed on the package, ensuring consistent concentrations of CBD • THC content is guaranteed to be lower than 0.3%
REGULATIONS	
• There are no federal standards for dispensary or online CBD products, and regulations vary by state	• Rx CBD (Epidiolex) is made according to WHO's Good Agriculture Practices and FDA's Good Manufacturing Practices
CLINICAL TRIALS	
• Non-Rx CBD products have not been tested in clinical trials	• Rx CBD (Epidiolex) was tested in numerous clinical trials to ensure it is effective and safe

PRACTICE AID

FDA-Approved Cannabidiol (CBD; Epidiolex) Patient Information Guide[1-4]

Full abbreviations, accreditation, and disclosure information available at **PeerView.com/Epilepsy2020**

PeerView INSTITUTE FOR MEDICAL EDUCATION

MLI Medical Learning Institute, Inc.

How Is CBD (Epidiolex) Taken?

- Oral liquid taken twice daily
- Administer consistently with respect to meals
- Can be taken by itself or in combination with other commonly prescribed seizure medications
- Doctor may start you on a lower dose and slowly increase the amount of medicine to reach the proper dose

What Is (and Is Not) in CBD (Epidiolex)?

- It is 100 mg/mL of cannabidiol in a sesame oil base
  - Sesame is a seed, not a nut
- No dairy or gluten
- No sugar or carbohydrates



How Should I Store CBD (Epidiolex)?

- Keep the bottle upright and use within 12 weeks after opening
- An unopened bottle expires 24 months after purchase
- Store at room temperature, between 68°F and 77°F
- Never freeze

Does CBD (Epidiolex) Interact With Other Medications?

- May interact with some seizure medicines, especially valproate and clobazam
- Other possible drug–drug interactions: acid reflux medicines, antibiotics, antidepressants, antifungals, antivirals, surgical anesthesia medicines, blood pressure/heart medicines, blood thinners

Important Safety Information

- Take CBD (Epidiolex) exactly as your healthcare provider tells you; do not stop taking without speaking to your healthcare provider, as stopping a seizure medicine suddenly can cause problems
- Most common side effects include an increase in liver enzymes, sleepiness, decreased appetite, diarrhea, fever, vomiting, feeling tired and weak, rash, sleep problems, and infections

CBD (Epidiolex) may also cause

- Suicidal thoughts or actions
- Harm to your unborn baby if you are pregnant
- Harm to your baby if you are breastfeeding
- Liver problems
  - Call your doctor with any of the following signs/symptoms: loss of appetite, nausea, vomiting; fever, feeling unwell, unusual tiredness; jaundice; itching; unusual darkening of the urine; right upper stomach area pain/discomfort

1. Epidiolex (cannabidiol) Prescribing Information. https://www.epidiolex.com/sites/default/files/pdfs/0820/EPX-03645-0820_EPIDIOLEX_%28cannabidiol%29_USPI.pdf. 2. https://www.epidiolex.com/sites/default/files/pdfs/EPX-04221-0420%20Downloadable%20EPIDIOLEX%20Brochure%20-%20Cannabinoids%20101-%20Understanding%20CBD.pdf. 3. https://www.epidiolex.com/sites/default/files/pdfs/0820/EPX-06380-0820%20EPIDIOLEX%20Quick%20Start%20Brochure.pdf. 4. https://www.cannabinoidclinical.com/themes/custom/cbed/pdf/medical-marijuana-discussion-guide.pdf.

PRACTICE AID

FDA-Approved Cannabidiol Oral Solution (CBD; Epidiolex) Quick Start Guide for Pharmacists

Full abbreviations, accreditation, and disclosure information available at **PeerView.com/Epilepsy2020**

PeerView INSTITUTE FOR MEDICAL EDUCATION

MLI Medical Learning Institute, Inc.

Dosage and Administration[1]

Dosage form: oral solution, 100 mg/mL

- LGS and DS
  - Starting dosage: 2.5 mg/kg twice daily
  - After 1 week, increase to 5 mg/kg twice daily
  - Maximum: 10 mg/kg twice daily (20 mg/kg daily)
- TSC
  - Starting dosage: 2.5 mg/kg twice daily
  - Increase dose weekly by 2.5 mg/kg twice daily, as tolerated, to recommended maintenance dosage of 12.5 mg/kg twice daily (25 mg/kg daily)
- Food may affect absorption, so consistent dosing with respect to meals is recommended, to reduce variability in CBD plasma exposure
- Can be administered via feeding tube if necessary

- Advise patients who are prescribed CBD (Epidiolex) to use adapter and oral dosing syringes provided
  - Wash and dry dosing syringe between uses, otherwise solution may turn cloudy
- Store CBD (Epidiolex) at room temperature between 68°F and 77°F (20°C to 25°C)
- Do **not** freeze
- Instruct patients to discard any unused CBD (Epidiolex) oral solution 12 weeks after opening bottle
- When discontinuing CBD (Epidiolex), dose should be decreased gradually to reduce risk of increased seizures and status epilepticus

PRACTICE AID

FDA-Approved Cannabidiol Oral Solution (CBD; Epidiolex) Quick Start Guide for Pharmacists

Full abbreviations, accreditation, and disclosure information available at **PeerView.com/Epilepsy2020**

PeerView INSTITUTE FOR MEDICAL EDUCATION

MLI Medical Learning Institute, Inc.

Safety and Monitoring[1]

The most common adverse reactions (10% or more for CBD [Epidiolex] and greater than placebo) in patients with LGS, DS, or TSC are

- CNS (somnolence, sedation, insomnia, poor quality sleep)
- GI (decreased appetite, diarrhea, vomiting)
- Hepatic (transaminase elevations)
- Dermatologic (rash)
- Infections
- Systemic (malaise, fatigue, asthenia, pyrexia)

- Monitor LFTs at baseline and at 1 month, 3 months, and 6 months after initiation and periodically thereafter, as clinically indicated
  - CBD (Epidiolex) can cause dose-related elevations of ALT and AST
    - » In 2/3 of cases, discontinuation or reduction of CBD (Epidiolex) resolved transaminase elevations
    - » In 1/3 of cases, elevations resolved without dose reduction of CBD (Epidiolex)
  - Dose adjustment recommended in patients with moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment
    - » Slower dose titration may be necessary
- Risk factors for transaminitis
  - Valproate cotherapy
  - High CBD (Epidiolex) dose
  - Elevated baseline transaminases

PRACTICE AID

FDA-Approved Cannabidiol Oral Solution (CBD; Epidiolex) Quick Start Guide for Pharmacists

Full abbreviations, accreditation, and disclosure information available at **PeerView.com/Epilepsy2020**

PeerView INSTITUTE FOR MEDICAL EDUCATION

MLI Medical Learning Institute, Inc.

Drug–Drug Interactions With CBD (Epidiolex)[1-3]

Category	Recommendations When Given Concomitantly With CBD (Epidiolex)	Examples
Moderate or strong inhibitors of CYP3A4 or CYP2C19	Consider dose reduction of CBD (Epidiolex)	Ketoconazole
Strong inducers of CYP3A4 or CYP2C19	Consider dose increase of CBD (Epidiolex)	Carbmazepine, phenytoin, rifampin
Substrates of UGT1A9, UGT2B7, CYP2C8, and CYP2C9	Consider dose reduction of substrates UGT1A9, UGT2B7, CYP2C8, and CYP2C9, as clinically appropriate, if adverse reactions are experienced	Diflunisal, propofol, lamotrigine, morphine, lorazepam, phenytoin, fenofibrate, gemfibrozil
Substrates of CYP1A2 and CYP2B6	Because of potential for both induction and inhibition of enzyme activity, consider adjusting dosage of substrates of CYP1A2 and CYP2B6, as clinically appropriate	Theophylline, caffeine, bupropion, efavirenz
Substrates of CYP2C19	Consider dose reduction of CYP2C19 substrate	Diazepam
Anti-seizure drugs that commonly interact with CBD (Epidiolex)	Concomitant use of CBD (Epidiolex) and valproate increases the incidence of liver enzyme elevations; if such elevations occur, discontinue or reduce CBD (Epidiolex) and/or concomitant valproate Concomitant use of CBD (Epidiolex) and clobazam may increase plasma concentration of N-desmethylclobazam 3-fold; consider reduction of clobazam dose if adverse reactions occur	Valproate, clobazam
Mammalian target of rapamycin (mTOR) or calcineurin inhibitors	Concomitant use of CBD (Epidiolex) and mTOR or calcineurin inhibitors may result in increased serum levels of mTOR or calcineurin inhibitors; consider a reduction in dosage of these drugs if adverse reactions occur	Everolimus, sirolimus, tacrolimus

1. Epidiolex (cannabidiol) Prescribing Information. https://www.epidiolex.com/sites/default/files/pdfs/0820/EPX-03645-0820_EPIDIOLEX_%28cannabidiol%29_USPI.pdf. 2. Stout SM, Cimino NM. *Drug Metab Rev.* 2014;46:86-95. 3. Gaston TE et al. *Epilepsia.* 2017;58:1586-1592.