The first and only

FDA-APPROVED PRESCRIPTION CANNABIDIOL[1]

Epidiolex® (cannabidiol) CV

FIRST IN A NEW CLASS OF AEDs THAT CONTAINS HIGHLY-PURIFIED CANNABIDIOL[1]

EPIDIOLEX® (cannabidiol) is indicated for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS) in patients 2 years of age and older. EPIDIOLEX is an oral solution supplied as 100 mL per bottle.[2]

Dosing

Starting dosage: 2.5 mg/kg twice daily (5 mg/kg/day)[2]

Recommended maintenance dosage: After 1 week, the dosage can be increased to 5 mg/kg twice daily (10 mg/kg/day)[2]

- Based on individual clinical response and tolerability, each dose can be further increased in weekly increments of 2.5 mg/kg administered twice daily (5 mg/kg/day) to 10 mg/kg twice daily (20 mg/kg/day)[2]
  - Administration of the 20 mg/kg/day dosage may cause an increase in adverse reactions
- Dose adjustment and slower dose titration is recommended in patients with moderate or severe hepatic impairment. Consider not initiating EPIDIOLEX in patients with evidence of significant liver injury[2]
  - Monitor within 1 month following changes in EPIDIOLEX dosage and addition of or changes in medications that are known to impact the liver

BENEFITS OF EPIDIOLEX

Structurally distinct from other AEDs

EPIDIOLEX, which lacks euphoric side effects associated with THC, is a novel AED that provides a different way to treat seizures.[2]

- While precise mechanisms are unknown, EPIDIOLEX is believed to exert its anticonvulsant effects through multiple modes of action
- Does not appear to exert its anticonvulsant effects through interaction with cannabinoid receptors

Significantly reduces seizures

The only AED approved for both LGS and Dravet syndrome; studied across 3 trials (N=516) in the **largest pivotal controlled clinical trial program to date** in the rare epilepsies LGS and Dravet syndrome.[2-9]

Has a safety and tolerability profile established in 3 clinical trials

The most common adverse reactions in patients receiving EPIDIOLEX (≥10% and greater than placebo) include somnolence; decreased appetite; diarrhea; transaminase elevations; fatigue, malaise, and asthenia; rash; insomnia, sleep disorder and poor-quality sleep; and infections. Hematologic abnormalities, decreased weight, and increased creatinine levels were also observed.[2]

Coverage and support

Eligible for insurance coverage and delivered to patients via specialty pharmacies.

MEETS FDA STANDARDS TO ENSURE CONSISTENT CONCENTRATIONS OF CANNABIDIOL

- Adheres to strict specifications, ensuring batch-to-batch consistency and stable shelf life, meeting all FDA standards[2]
- Produced according to regulated current Good Manufacturing Practice (cGMP) and Good Agricultural Practice (GAP)[10]
- 100% of plants grown in highly regulated state-of-the-art greenhouses[10]
  - No pesticides, no contaminants, no heavy metals, and not genetically modified

Visit **EPIDIOLEXhcp.com** for more details.

Please see full Important Safety Information on next page and full Prescribing Information at EPIDIOLEXhcp.com.

IMPORTANT SAFETY INFORMATION & INDICATIONS

Contraindication: Hypersensitivity

EPIDIOLEX (cannabidiol) oral solution is contraindicated in patients with a history of hypersensitivity to cannabidiol or any ingredients in the product.

Warnings & Precautions

Hepatocellular Injury:

EPIDIOLEX can cause dose-related transaminase elevations. Concomitant use of valproate and elevated transaminase levels at baseline increase this risk. Transaminase and bilirubin levels should be obtained prior to starting treatment, at one, three, and six months after initiation of treatment, and periodically thereafter, or as clinically indicated. Resolution of transaminase elevations occurred with discontinuation of EPIDIOLEX, reduction of EPIDIOLEX and/or concomitant valproate, or without dose reduction. For patients with elevated transaminase levels, consider dose reduction or discontinuation of EPIDIOLEX or concomitant medications known to affect the liver (e.g., valproate or clobazam). Dose adjustment and slower dose titration is recommended in patients with moderate or severe hepatic impairment. Consider not initiating EPIDIOLEX in patients with evidence of significant liver injury.

Somnolence and Sedation:

EPIDIOLEX can cause somnolence and sedation that generally occurs early in treatment and may diminish over time; these effects occur more commonly in patients using clobazam and may be potentiated by other CNS depressants.

Suicidal Behavior and Ideation:

Antiepileptic drugs (AEDs), including EPIDIOLEX, increase the risk of suicidal thoughts or behavior. Inform patients, caregivers, and families of the risk and advise to monitor and report any signs of depression, suicidal thoughts or behavior, or unusual changes in mood or behavior. If these symptoms occur, consider if they are related to the AED or the underlying illness.

Withdrawal of Antiepileptic Drugs:

As with most AEDs, EPIDIOLEX should generally be withdrawn gradually because of the risk of increased seizure frequency and status epilepticus.

Adverse Reactions:

The most common adverse reactions in patients receiving EPIDIOLEX (≥10% and greater than placebo) include somnolence; decreased appetite; diarrhea; transaminase elevations; fatigue, malaise, and asthenia; rash; insomnia, sleep disorder and poor-quality sleep; and infections. Hematologic abnormalities were also observed.

Pregnancy:

EPIDIOLEX should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Encourage women who are taking EPIDIOLEX during pregnancy to enroll in the North American Antiepileptic Drug (NAAED) Pregnancy Registry.

Drug Interactions:

Moderate or strong inhibitors or inducers of CYP3A4 and CYP2C19 may affect EPIDIOLEX exposure. EPIDIOLEX may affect exposure to CYP2C19 substrates (e.g. clobazam, diazepam) or others. Concomitant use of EPIDIOLEX and valproate increases the incidence of liver enzyme elevations. Dosage adjustment of EPIDIOLEX or other concomitant medications may be necessary.

Drug Abuse:

EPIDIOLEX is a Schedule V controlled substance and has a low potential for abuse.

Indications:

EPIDIOLEX is indicated for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS) in patients 2 years of age and older.

Please refer to the EPIDIOLEX full Prescribing Information for additional important information.

References: 1. FDA approves first drug comprised of an active ingredient derived from marijuana to treat rare, severe forms of epilepsy. Food and Drug Administration website. https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm611046.htm. Accessed June 29, 2018. **2.** EPIDIOLEX [package insert]. Carlsbad, CA: Greenwich Biosciences, Inc.; 2018. **3.** BANZEL [package insert]. Woodcliff Lake, NJ: Eisai Inc.; 2015. **4.** TOPAMAX [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; 2018. **5.** ONFI [package insert]. Deerfield, IL: Lundbeck; 2018. **6.** FELBATOL [package insert]. Somerset, NJ: Meda Pharmaceuticals; 2011. **7.** DIACOMIT [package insert]. Beauvais, France: Biocodex; 2018. **8.** Sullivan J, Lagae L, Knupp K, et al. Effect of ZX008 (fenfluramine HCl oral solution) on total seizures in Dravet syndrome in a phase 3 clinical trial. Poster presented at: American Acadamy of Neurology Annual Meeting; April 2018; Los Angeles, CA. **9.** Zogenix announces positive top-line results from second pivotal phase 3 clinical trial of ZX008 in Dravet syndrome. Zogenix website. https://zogenixinc.gcs-web.com/news-releases/news-release-details/zogenix-announces-positive-top-line-results-second-pivotal-phase. Accessed August 1, 2018. **10.** Data on file. Greenwich Biosciences, Inc., Carlsbad, CA.

GREENWICH™ BIOSCIENCES

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