Epidiolex® (cannabidiol) – New drug approval

- On June 25, 2018, GW Pharmaceuticals and its U.S. subsidiary Greenwich Biosciences announced the FDA approval of Epidiolex (cannabidiol), for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS) in patients 2 years of age and older.
    - Before Epidiolex may be made available to patients, it must be rescheduled from its current Schedule 1 status. The rescheduling will likely occur within 90 days.
- LGS and DS, which develop in childhood, are rare, severe forms of epilepsy that are notoriously treatment-resistant. Most patients with LGS and DS require multiple seizure medications and the majority are resistant to currently approved anti-epileptic drugs. There are high rates of early mortality associated with both syndromes.
    - According to the DS Foundation, DS affects 1:15,700 individuals.
    - According to the LGS Foundation, LGS has a prevalence of 30,000 - 50,000 children and adults in the U.S.
- Epidiolex is the first prescription pharmaceutical formulation of highly-purified, plant-derived cannabidiol. This cannabinoid lacks the high associated with marijuana.
- The efficacy of Epidiolex for the treatment of seizures associated with LGS was demonstrated in two placebo-controlled studies enrolling 396 patients. The primary efficacy measure in both studies was the percent change from baseline in the frequency (per 28 days) of drop seizures (atonic, tonic, or tonic-clonic seizures) over the 14-week treatment period.
    - In study 1, the median percent change in drop seizure frequency was -22% for placebo patients vs. -44% for Epidiolex-treated patients ($p = 0.01$).
    - In study 2, the median percent change in drop seizure frequency was -17% for placebo patients, -37% for Epidiolex 10 mg/kg/day patients, and -42% for Epidiolex 20 mg/kg/day patients ($p < 0.01$ for both Epidiolex-treated groups vs. placebo).
- The efficacy of Epidiolex for the treatment of DS was demonstrated in a placebo-controlled study enrolling 120 patients aged 2 – 18 years. The primary efficacy measure was the percent change from baseline in the frequency (per 28 days) of convulsive seizures (all countable atonic, tonic, clonic, and tonic-clonic seizures) over the 14-week treatment period.
    - The median percent change in convulsive seizure frequency was -13% for placebo patients vs. -39% for Epidiolex-treated patients ($p = 0.01$).
- Warnings and precautions of Epidiolex include hepatocellular injury, somnolence and sedation, suicidal behavior and ideation, hypersensitivity reactions, and withdrawal of antiepileptic drugs.
- The most common adverse reactions (≥ 10% and > placebo) with Epidiolex use were somnolence; decreased appetite; diarrhea; transaminase elevations; fatigue, malaise, and asthenia; rash; insomnia, sleep disorder, and poor quality sleep; and infections.
- The recommended starting dosage of Epidiolex is 2.5 mg/kg orally twice daily (5 mg/kg/day). After one week, the dosage can be increased to a maintenance dosage of 5 mg/kg orally twice daily (10 mg/kg/day).

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- — Patients who are tolerating Epidiolex at 5 mg/kg twice daily and require further reduction of seizures may benefit from a dosage increase up to a maximum recommended maintenance dosage of 10 mg/kg twice daily (20 mg/kg/day), in weekly increments of 2.5 mg/kg twice daily (5 mg/kg/day), as tolerated.
- — For patients in whom a more rapid titration from 10 mg/kg/day to 20 mg/kg/day is warranted, the dosage may be increased no more frequently than every other day.
- — Administration of the 20 mg/kg/day dosage resulted in somewhat greater reductions in seizure rates than the recommended maintenance dosage of 10 mg/kg/day, but with an increase in adverse reactions.
- — Serum transaminases (ALT and AST) and total bilirubin levels should be obtained in all patients prior to starting treatment with Epidiolex.

- Greenwich Biosciences launch plans for Epidiolex are pending. Epidiolex will be available as a 100 mg/mL oral solution.