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Gerd W. Clabaugh, Director
Iowa Department of Public Health
Lucas Office Building
Des Moines, IA 50319

Re: Report FY 2018- Report on Use of Medical Cannabidiol

Dear Members of the Iowa General Assembly and Director Clabaugh:

Pursuant to the 2014 Iowa Acts Ch 1125, §10h, enclosed is the report on Report on Use of Medical Cannabidiol.

If you have any questions or need more information, please don't hesitate to contact this office.

Sincerely,

Mark J. Braun

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Attachments
cc: Robin Madison
Legislative Liaisons
Legislative Log

University of Iowa Children's Hospital
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July 12th, 2019
University of Iowa

Re: **2019 Report to the Department of Public Health and the Iowa General Assembly**

Recent Publications and additions since the last review submitted July 2017:

There have only been 3 randomized placebo-controlled trials published since the last review.

- The first was published by Devinsky and coworkers [1] in 2017 in the New England Journal of Medicine. In this double-blind, placebo-controlled trial, they randomly assigned 120 children and young adults with the Dravet syndrome and drug-resistant seizures to receive either cannabidiol oral solution at a dose of 20 mg per kilogram of body weight per day or placebo, in addition to standard antiepileptic treatment. The patients with Dravet syndrome and who were treated with cannabidiol resulted in a greater reduction in convulsive-seizure frequency than placebo, however, they also had higher rates of adverse events.
- The second study, was also published by Devinsky and coworkers [2] in 2018 in the New England Journal of Medicine. In this double-blind, placebo-controlled trial conducted at 30 clinical centers, they randomly assigned 225 patients with the Lennox-Gastaut syndrome (age range, 2 to 55 years) who had had two or more drop seizures per week during a 28-day baseline period to receive cannabidiol oral solution at a dose of either 20 mg per kilogram of body weight (20-mg cannabidiol group) or 10 mg per kilogram (10-mg cannabidiol group) or matching placebo. Among children and adults with the Lennox-Gastaut syndrome, the addition of cannabidiol at a dose of 10 mg or 20 mg per kilogram per day to a conventional antiepileptic regimen resulted in greater reductions in the frequency of drop seizures than placebo. Adverse events with cannabidiol included elevated liver aminotransferase concentrations.
- The third study was published by Thiele and colleagues [3] also in 2018 in the journal Lancet. In this randomized, double-blind, placebo-controlled trial done at 24 clinical sites in the USA, the Netherlands, and Poland, they investigated the efficacy of cannabidiol as add-on therapy for drop seizures in patients with treatment-resistant Lennox-Gastaut syndrome. They concluded that add-on cannabidiol is efficacious for the treatment of patients with drop seizures associated with Lennox-Gastaut syndrome and is generally well tolerated.

Based on these 3 studies the U.S. Food and Drug Administration granted approval of Epidiolex® (brand of oral cannabidiol solution for the treatment of intractable epilepsy associated with Dravet Syndrome and Lennox-Gastaut Syndrome in individuals 2 years and older. The approval was granted June 25, 2018. However, the Drug Enforcement Agency (DEA) had to determine the schedule for this new drug.

A study was published in 2018 in Epilepsy Behavior by Schoedel and coworkers [4]. They evaluated the abuse potential of cannabidiol in a single-dose, randomized, double-blind, double-dummy, placebo- and active-controlled crossover trial. The abuse potential of single oral doses of plant-derived pharmaceutical formulations of highly purified CBD (Epidiolex®; 750mg, 1500mg, and 4500mg) was compared with that of single oral doses of alprazolam (2mg), dronabinol (10mg and 30mg), and placebo in healthy recreational polydrug users. Administration of a therapeutic dose of CBD (750mg) showed significantly low abuse potential in a

highly sensitive population of polydrug users. Although high and supratherapeutic doses of CBD (1500mg and 4500mg, respectively) had detectable subjective effects compared with placebo; the effects were significantly lower than those observed with alprazolam and dronabinol. The DEA used this study to make the determination that cannabidiol oral solutions that contain no more than 0.1% tetrahydrocannabinol (THC) be reclassified from Schedule 1 to Schedule 5, indicating that they have some, but limited potential for abuse. This ruling was published in the Federal Register September 28, 2018.

The University of Iowa Carver College of Medicine and the University of Iowa College of Pharmacy recommends that based on the approval of oral cannabidiol solution for the treatment of these two epileptic seizure disorders that this new prescription product be used instead of the oral cannabidiol/medical marijuana products produced by the State of Iowa for the treatment of epilepsy. The new prescription product should be covered by Medicare and most private insurance programs; whereas the state products are costly and not covered by Medicare or private insurance.

References

1. Devinsky, O., et al., *Trial of Cannabidiol for Drug-Resistant Seizures in the Dravet Syndrome.* N Engl J Med, 2017. **376**(21): p. 2011-2020.
2. Devinsky, O., et al., *Effect of Cannabidiol on Drop Seizures in the Lennox-Gastaut Syndrome.* N Engl J Med, 2018. **378**(20): p. 1888-1897.
3. Thiele, E.A., et al., *Cannabidiol in patients with seizures associated with Lennox-Gastaut syndrome (GWPCARE4): a randomised, double-blind, placebo-controlled phase 3 trial.* Lancet, 2018. **391**(10125): p. 1085-1096.
4. Schoedel, K.A., et al., *Abuse potential assessment of cannabidiol (CBD) in recreational polydrug users: A randomized, double-blind, controlled trial.* Epilepsy Behav, 2018. **88**: p. 162-171.

Ronald A. Herman

Sincerely,

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Sincerely,

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