Exploring the Use of Electronic Health Records (EHR) Data for Active Safety Surveillance of Epidiolex® in PCORnet®, July 1, 2018- July 1, 2022

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Silvia Perez-Vilar[1], Sara Karami[1], Christine Draper[2], Karen Long[1], Kimberly Barrett[2], Kira Leishear[1], Kshema Nagavedu[2], Rose Radin[1], Emma Hoffman[2], Patty Greene[1], Ashley I. Martinez[2], Jana Mcaninch[1], Sheryl A. Kluberg[2]

[1]Office of Surveillance and Epidemiology, Center for Drug Evaluation and Research, U.S. Food and Drug Administration

[2]Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute

Background

In June 2018, the US Food and Drug Administration (FDA) approved the first cannabis-derived cannabidiol (CBD) human drug product (Epidiolex®), currently indicated for the treatment of seizures associated with Lennox-Gastaut syndrome, Dravet syndrome, or tuberous sclerosis complex in patients ages ≥1 year [1]. In December 2018, the Agriculture Improvement Act of 2018, also known as the 2018 Farm Bill, legalized hemp, defined as cannabis (Cannabis sativa L.) and derivatives of cannabis with low concentrations of the psychoactive compound delta-9-tetrahydrocannabinol (THC) (no more than 0.3 percent THC on a dry weight basis), hemp was removed from the definition of marijuana in the Controlled Substances Act (CSA). Since then, the CBD market has rapidly increased in volume and complexity, spanning thousands of products, including Epidiolex® and non-FDA approved products marketed as drugs, foods, cosmetics, and dietary supplements [2].

Objective

To explore the use of PCORnet®, the National Patient-Centered Clinical Research Network, for active safety surveillance of Epidiolex®.

Methods

We conducted this descriptive analysis in the FDA's Sentinel System using data from 23 DataMarts in PCORnet®, an electronic health records-based network of networks that uses a common data model. The sites represented academic and community health care systems serving self-pay or publicly or privately insured patients. We required patients to have ≥1 encounter prior to the exposure of interest (day 0) between July 1, 2018, through July 1, 2022, to define the following exposure-based cohorts: (1) Epidiolex®, (2) CBD (no brand name), (3) Hemp, including CBD (excluding Epidiolex®). We assessed demographics, clinical characteristics (days [-365, 0]), medications (days [-30, 30]), and healthcare utilization (days [-365, -1]). We used RxNorm Concept Unique Identifier (RXCUI) and National Drug Codes (NDC) to identify exposures and Current Procedural Terminology (CPT), Healthcare Common Procedure Coding System (HCPCS) Codes, International Classification of Diseases, Ninth and Tenth Revision, Clinical Modification (ICD-9-CM and ICD-10-CM), International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS), RXCUI, and NDC to define baseline characteristics. We requested the execution of the query using the PCORnet Modular Program (PMP) tool, version v2.1 on August 24, 2022.

Results

Table 1. Demographic Characteristics and Healthcare Utilization of Individuals with Exposure to Epidiolex, CBD (no Brand Name), and/or Hemp (Excluding Epidiolex®) in the Medication Records, PCORnet®

	Epidiolex®	Cannabidiol (no brand name)	Hemp (including non-Epidiolex® CBD)
Number of Unique Patients	6,306	2,558	2,573
Demographics (Day 0)			
Mean age (SD)	27.2 (17.1)	36.8 (24.0)	36.9 (24.0)
Female	3,207 (51%)	1,403 (55%)	1,407 (55%)
White	5,168 (82%)	1,903 (74%)	1,918 (75%)
Black or African American	475 (8%)	213 (8%)	213 (8%)
Non-Hispanic Ethnicity	5,336 (85%)	1,971 (77%)	1,986 (77%)
Area Deprivation Index Quartile*			
Q1 (least deprivation)	2,269 (36%)	759 (30%)	767 (30%)
Q2	1,570 (25%)	707 (28%)	709 (28%)
Q3	1,435 (23%)	552 (22%)	555 (22%)
Q4 (most deprivation)	922 (15%)	536 (21%)	538 (21%)
Healthcare Utilization, Days (-365, -1)			
Emergency Care Setting	1,209 (19%)	347 (14%)	353 (14%)
Inpatient (IP, OS, or EI) Care Setting	2,039 (32%)	487 (19%)	492 (19%)

*Area Deprivation Index (ADI) is a proxy measure for socioeconomic status to capture patient-level social risk factors

Abbreviations: 'EI'=Emergency Department Admit to Inpatient Hospital Stay; 'IP'=Inpatient; 'OS'=Observation Stay; 'Q'= quarter; 'SD'=standard deviation.

Table 2. Selected Clinical Characteristics and Medications of Individuals with Exposure to Epidiolex, CBD (no Brand Name), and/or Hemp (Excluding Epidiolex®) in the Medication Records, PCORnet®

	Epidiolex®	Cannabidiol (no brand name)	Hemp (including non-Epidiolex® CBD)
Number of Unique Patients	6,306	2,558	2,573
Clinical Characteristics, Days (-365, 0)			
Epilepsy (Dravet, Lennox-Gastaut, Tuberous Sclerosis Complex)	1,959 (31%)	523 (20%)	523 (20%)
Other Epilepsies and Seizure Disorders	4,131 (66%)	1,276 (50%)	1,277 (50%)
Neurological Conditions	4,120 (65%)	1,313 (51%)	1,316 (51%)
Anxiety Disorders	967 (15%)	352 (14%)	355 (14%)
Sleep Disorders	1,287 (20%)	443 (17%)	450 (17%)
Psychosis or Psychotic Disorders	63 (1%)	27 (1%)	27 (1%)
Cancer	322 (5%)	220 (9%)	225 (9%)
Diabetes	271 (4%)	125 (5%)	128 (5%)
Hypertension	785 (12%)	380 (15%)	387 (15%)
Pulmonary Disease	666 (11%)	275 (11%)	277 (11%)
Substance Use Disorder	158 (3%)	71 (3%)	72 (3%)
Medications, Days (-30, 30)			
Anticonvulsants	4,462 (71%)	1,267 (50%)	1,276 (50%)
Antidepressants	1,046 (17%)	300 (12%)	305 (12%)
Antiemetics	1,052 (17%)	316 (12%)	324 (13%)
Anxiolytics	1,915 (30%)	416 (16%)	423 (16%)
Opioids	715 (11%)	234 (9%)	245 (10%)

Discussion

Although some of the differences might be explained by the younger mean age in the Epidiolex® cohort, overall, the cohorts did not differ by other demographics, clinical characteristics, medications, or healthcare utilization, suggesting that most CBD exposures (and most hemp exposures) identified correspond to Epidiolex®. Although further explorations are needed, results suggest that, when using PCORnet® for active surveillance of Epidiolex® using structured fields (prescription, dispensing, and medication administration information), we should consider including both CBD exposures with and without a brand name in order to capture Epidiolex® exposures that might be otherwise overlooked.

References

[1] US Food and Drug Administration. Package insert. Epidiolex®; GW Research, Ltd. 2022 [updated February 24, 2022].

[2] US Food and Drug Administration. Cannabis Derived Products Data Acceleration Plan. Exploring Novel Data Sources to Help Inform Cannabis Derived Product Safety and Quality Gaps 2021 [updated October 16, 2021]

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