An analysis of adverse events reported for cannabis-derived and synthetic cannabis-related drug products using the FDA Adverse Event Reporting System (FAERS)

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Introduction

- There are several **cannabis-derived (i.e., Epidiolex®, cannabidiol)** and **synthetic cannabis-related (i.e., Marinol®, Syndros®, Cesamet™, Sativex®)** drug products on the market.
- No studies to date have comprehensively reviewed safety profiles, including reported **adverse drug events (ADEs)**, for cannabis-derived and synthetic products approved in the United States and internationally.

Objective

To examine ADE reports for cannabis-derived, synthetic cannabis-related, and unspecified cannabidiol (CBD) drug products, and to describe ADE reports by characteristics, reactions, and outcomes reported.

Methods

- **Data:** FDA Adverse Event Reporting System (FAERS)
- **Timeframe:** 1985 to 2019, Quarter 3
- **Drugs:** brand and generic product names as well as common names (e.g., "CBD") used to extract reports
- **Characteristics of the ADE:** cannabinoid product's role in the event, sex, and outcomes
- **Reactions:** described by Medical Dictionary for Regulatory Activities (MedDRA) Preferred Terms
- **Analysis:** descriptive statistics, SAS v.9.4

Results

Unique ADE reports	n	Most frequent reaction by product*
Marinol® or Syndros®	1,892	Death (4.9%)
Epidiolex®	655	Seizure (26.0%)
Cesamet™	374	Therapeutic product effect incomplete (7.5%)
Sativex®	183	Multiple sclerosis relapse (7.1%)
Unspecified CBD	341	Off-label use (3.8%)

*Listen to the recording for other frequently reported reactions!

Characteristics and Outcomes of ADE reports, overall and by drug product

n (%)	Total reports	Marinol®/Syndros® (dronabinol)	Epidiolex® (cannabidiol)	Cesamet® (nabilone)	Sativex® (nabiximols)	Unspecified CBD
# of ADE reports	3,445	1,892 (54.9)	655 (19.0)	374 (10.9)	183 (5.3)	341 (9.9)
Sex, female†	1,351 (39.2)	801 (42.3)	25 (3.8)	220 (58.8)	117 (63.9)	188 (55.1)
Drug product's role in the event						
Primary or secondary suspect	1,290 (37.4)	454 (24.0)	633 (96.6)	110 (29.4)	25 (13.7)	68 (19.9)
Concomitant or interacting	1,636 (47.5)	1,428 (76.0)	22 (3.4)	264 (70.6)	158 (86.3)	273 (80.1)
Outcomes						
Hospitalization	1,408 (40.9)	777 (41.1)	321 (49.0)	123 (32.9)	95 (51.9)	92 (27.0)
Other serious‡	1,327 (38.5)	584 (30.9)	273 (41.7)	205 (54.8)	60 (32.8)	205 (60.1)
Death	577 (16.8)	467 (24.7)	53 (8.1)	29 (7.8)	10 (5.5)	18 (5.3)
Disability	68 (2.0)	31 (1.6)	4 (0.6)	10 (2.7)	10 (5.5)	13 (3.8)
Life-threatening	49 (1.4)	22 (1.2)	4 (0.6)	3 (0.8)	8 (4.6)	12 (3.5)
Congenital abnormality	16 (0.5)	11 (0.6)	---	4 (1.1)	---	1 (0.3)

†Missing, sex: total 22.8%; Marinol/Syndros 4.2%; Epidiolex 92.4%; Cesamet 15.0%; Sativex 2.7%; other CBD 11.4%

‡Other serious defined by FDA as important medical events, when the event does not fit the other outcomes, but may jeopardize the patient and may require medical or surgical intervention.

Overall, the most frequently reported **reactions** were **seizure**, **death**, and **decreased appetite**.

The most frequent **outcomes** were **hospitalizations**, **serious medical events**‡, and **death**.

Discussion & Conclusion

- The product's role in the ADE was as concomitant or interacting more frequently than as a primary or secondary suspect, with the exception of Epidiolex®.
- **Most frequently reported reactions were related to the indications for which the products are approved**.
- **Death** was the second most frequent reaction overall and which **accounted for one in six reported outcomes**.
- Limitations: ADEs and outcomes are prone to reporting bias and have not been assessed by the FDA for causality; reports from international countries are limited.

Presence of the most frequent ADEs and outcomes warrants further safety evaluation.

References

1. FDA Adverse Event Reporting System & terminology: https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program
2. Cannabis-derived & synthetic cannabis-related products: https://www.fda.gov/news-events/public-health-focus/fda-and-cannabis-research-and-drug-approval-process
3. Icons made by Freepik from www.flaticon.com

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Disclosures Statement

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