

# Some Things to Know When Using Cannabis-derived Products



Cannabis and hemp products contain many active ingredients, such as **CBD**, **THC**, and others.<sup>1</sup>



Both CBD and THC **can interact** with common medicines.<sup>2,6,8-10</sup>




**FDA approval** requires assessment of benefits and risks of a product.<sup>3</sup> FDA also inspects manufacturing.<sup>4</sup>


**If products do not go through an FDA review, it can be difficult to predict their interactions with other drugs.<sup>5</sup> It is important to tell your healthcare provider about all the products you are taking.**


**Based on the 4 FDA-approved CBD or THC drugs, CBD and THC may have the following side effects and drug-drug interactions in the conditions studied:**


CBD


POTENTIAL SIDE EFFECT(S)<sup>\*6</sup>


  
Liver problems


  
Drowsiness

  
Fatigue

  
Abnormal sleep

  
Diarrhea

  
Decreased appetite

  
Rash

CBD


POSSIBLE DRUG-DRUG INTERACTION(S)<sup>\*2,7</sup>


- > Acid reflux medicines
- > Antibiotics
- > Antidepressants
- > Anti-seizure medicines
- > Antifungals


- > Antivirals
- > Surgical anesthesia medicines
- > Blood pressure/heart medicines
- > Blood thinners


THC


POTENTIAL SIDE EFFECT(S)<sup>\*8-10</sup>


  
Dizziness

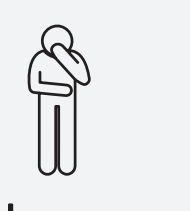
  
Drowsiness


  
Abnormal thoughts

  
Paranoia

  
Euphoria

  
Abdominal pain

  
Nausea

  
Vomiting

THC

POSSIBLE DRUG-DRUG INTERACTION(S)<sup>\*8-10</sup>

- > Antibiotics
- > Anti-seizure medicines
- > Antifungals

- > Antivirals
- > Pain medicines
- > Cancer medicines

\*This is a general list of possible interactions with these types of medications; it is not a complete list of all potential side effects or drug interactions.

## DID YOU KNOW?



The FDA has issued at least 96 warning letters to dispensary companies for incorrect labels and illegal advertising.<sup>\*\*11</sup>



Multiple studies of non-FDA-approved products showed nearly 2/3 were mislabeled for CBD and another 1/5 contained undisclosed THC.<sup>†12-14</sup>



A study of non-FDA-approved edible CBD products showed that more than 40% contained varying amounts of lead and nearly 30% contained varying amounts of arsenic.<sup>†12</sup>



FDA-approved products containing CBD or THC have undergone rigorous testing.<sup>15</sup>

**Talk to your healthcare provider if you are using cannabis and/or hemp products.**

If you have additional questions, Jazz Pharmaceuticals Medical Information department may be reached by email [medinfo@greenwichbiosciences.com](mailto:medinfo@greenwichbiosciences.com) or by calling 1-833-424-6724.

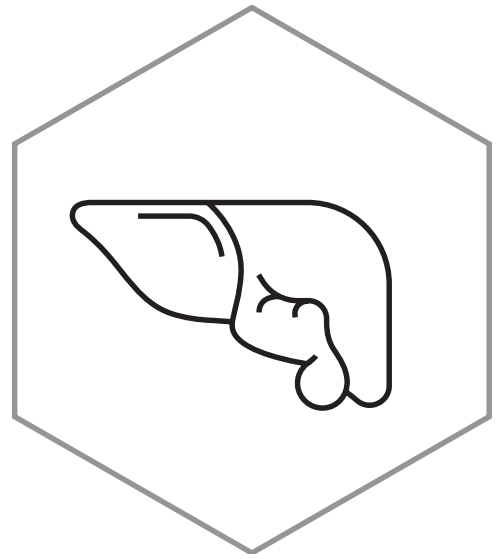
\*\*Based on warning letters sent from 2015 to September 2022. Warning letters were issued by the FDA when a company did not accurately state the contents of the THC or CBD product it was promoting. Letters were also issued by the FDA when a company made a misleading medical claim.

†In this study, 84 different products containing a cannabinoid (such as CBD or THC) were purchased. Then, researchers from the University of Pennsylvania Perelman School of Medicine examined each product to test whether the actual contents matched what was stated on the label.

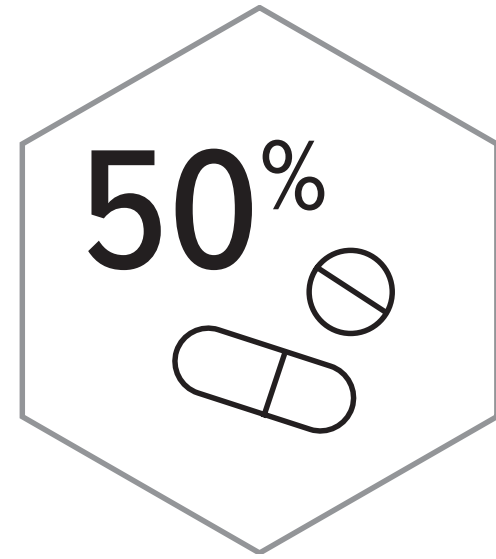
†In this study, 516 different products containing cannabinoids, 121 edible and 395 topical formulations, were purchased. Then, researchers examined each product to test whether the actual contents matched what was stated on the label.

1. Yang Y, Lewis MM, Bello AM, Wasilewski E, Clarke HA, Kotra LP. Cannabis sativa (Hemp) Seeds, Delta(9)-Tetrahydrocannabinol, and Potential Overdose. *Cannabis Cannabinoid Res.* 2017;2(1):274-281. 2. IBM Micromedex® DRUGDEX® (electronic version). IBM Watson Health. Sep 1, 2022. 3. US Food and Drug Administration. Step 3: Clinical Research. FDA.gov. Accessed Sep 1, 2022. 4. US Food and Drug Administration. Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients Guidance for Industry. Accessed Dec 3, 2021. 5. Kocis PT, Vrana KE, Delta-9-Tetrahydrocannabinol and Cannabidiol Drug-Drug Interactions. *Med Cannabis Cannabinoids.* 2020 Aug;3(1):61-73. 6. Epidiolex® (cannabidiol) oral solution [package insert]. Carlsbad, CA: Greenwich Biosciences, Inc. 7. Balachandran P, Elsohly M, Hill KP. Cannabidiol Interactions with Medications, Illicit Substances, and Alcohol: a Comprehensive Review. *J Gen Intern Med.* 2021 Jul;36(7):2074-2084. 8. Marinol® (dronabinol) capsules, for oral use [package insert]. North Chicago, IL: AbbVie Inc. 9. Cesamet® (nabilone) capsules [package insert]. Bridgewater, NJ: Bausch Health US LLC. 10. Syndros® (dronabinol) oral solution [package insert]. Chandler, AZ: Benuvia Therapeutics Inc. 11. US Food and Drug Administration. Warning Letters and Test Results for Cannabidiol-Related Products. FDA.gov. Updated May 6 2022. Accessed Sep 1, 2022. 12. Gardener H, Wallin C, Bowen J. Heavy metal and phthalate contamination and labeling integrity in a large sample of US commercially available cannabidiol (CBD) products. *Science of The Total Environment.* 2022 2022/12/10;/851:158110. 13. Bonn-Miller MO, Loflin MJE, Thomas BF, Marcu JP, Hyke T, Vandrey R. Labeling Accuracy of Cannabidiol Extracts Sold Online. *JAMA.* 2017 Nov 7;318(17):1708-1709. 14. Johnson E, Kilgore M, Babalonis S. Cannabidiol (CBD) product contamination: Quantitative analysis of delta-9-tetrahydrocannabinol (delta-9-THC) concentrations found in commercially available CBD products. *Drug and Alcohol Dependence.* 2022 2022/08/01;/237:109522. 15. US Food and Drug Administration. FDA and Cannabis: Research and Drug Approval Process. Updated Oct 10. Accessed Sept 2, 2021.

# Importance of Monitoring Drug Interactions Between Your Patients' Medications and Cannabis Products



The **cytochrome P-450 (CYP) system** is one of the most important systems for drug metabolism.<sup>1</sup>



Approximately **50%** of all clinically prescribed drugs are metabolized via CYP3A4.<sup>1</sup>



**Cannabinoid products** are cleared by the CYP-450 system, including CYP3A4.<sup>2-5</sup>

## Based on the 4 FDA-approved cannabinoid drugs:

- CBD is a substrate for CYP3A4 and CYP2C19.<sup>2</sup> THC is a substrate for CYP3A4 and CYP2C9.<sup>3-5</sup> Drugs that inhibit or induce these enzymes will affect the plasma concentrations of CBD and THC.<sup>2,3,5</sup>
- CBD and THC can function as inhibitors, inducers, or both.<sup>2-5</sup>
- CBD and THC are highly protein bound and may displace other drugs, increasing the risk of adverse events.<sup>2-5</sup>



**Health care providers should consider monitoring patient's use of cannabinoid-based products to reduce the risk of adverse events and to maintain the effectiveness of other concomitant medications.**

As CBD and THC are metabolized by the CYP450 System, the inhibition and/or induction of these enzymes by **other drugs may change plasma concentrations of CBD/THC.**<sup>2-7\*</sup>

> Antiarrhythmics  
> Antibiotics  
> Anticonvulsants

> Antidepressants  
> Antifungals  
> Antihypertensives

> Antiplatelets  
> Antivirals  
> Proton pump inhibitors

> Sympathomimetics  
> Others

Provider's discretion in identifying potential drug interactions as well as monitoring for safety and effectiveness is recommended.

\*Not a complete list of drug-drug interactions.

**CBD and THC may also change plasma concentrations of other drugs due to their own effects on metabolic enzymes and transport proteins.\***

	CBD <sup>2</sup>		THC <sup>8,9</sup>	
	Inhibition	Induction	Inhibition	Induction
<b>CYP1A2:</b> Antipsychotics, Antidepressants, Asthmatics, NSAIDs <sup>1</sup>	✓			
<b>CYP2B6:</b> Antidepressants, Chemotherapy, Opioids <sup>1</sup>	✓	✓		
<b>CYP2C8:</b> Diuretics, Chemotherapy, Hypoglycemics <sup>1</sup>	✓			
<b>CYP2C9:</b> Antihypertensives, NSAIDs, Hypoglycemics, Anticoagulants <sup>10</sup>	✓		✓†	✓†
<b>CYP2C19:</b> Proton pump inhibitors, Anticonvulsants <sup>10</sup>	✓			
<b>UGT1A9:</b> NSAIDs, Antilipemics, General Anesthetics <sup>2</sup>	✓			
<b>UGT2B7:</b> Anticonvulsants, Opioids, Antilipemics <sup>2</sup>	✓			
<b>P-gp:</b> Anticoagulants, Cardiac glycosides <sup>11</sup>	✓			

Therapeutic classes listed are examples of enzyme substrates.

†Disclaimer - There is evidence that other isoenzymes have been inhibited or induced by THC however, data are inconclusive

**Advise patients to talk to their health care providers about their current medications and OTC products they are taking at their next visit.**

**Pharmacists should talk to their patients at their next visit about possible drug interactions with concomitant cannabinoid therapy.**

If you have additional questions, Jazz Pharmaceuticals Medical Information department may be reached by email [medinfo@greenwichbiosciences.com](mailto:medinfo@greenwichbiosciences.com) or by calling 1-833-424-6724.

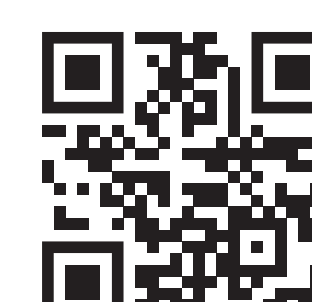
1. Guengerich FP. Human Cytochrome P450 Enzymes. In: Ortiz de Montellano PR, ed. *Cytochrome P450*. Springer International Publishing; 2015:523-785:chap Chapter 9. 2. Epidiolex® (cannabidiol) oral solution [package insert]. Carlsbad, CA: Greenwich Biosciences, Inc. 3. Syndros® (dronabinol) oral solution [package insert]. Chandler, AZ: Benuvia Therapeutics Inc. 4. Cesamet® (nabilone) capsules [package insert]. Bridgewater, NJ: Bausch Health US LLC. 5. Marinol® (dronabinol) capsules, for oral use [package insert]. North Chicago, IL: AbbVie Inc. 6. IBM Micromedex® DRUGDEX® (electronic version). IBM Watson Health. Sep 1, 2022. 7. Balachandran P, Elsohly M, Hill KP. Cannabidiol Interactions with Medications, Illicit Substances, and Alcohol: a Comprehensive Review. *J Gen Intern Med*. 2021 Jul;36(7):2074-2084. 8. Doohan PT. Cannabinoid Interactions with Cytochrome P450 Drug Metabolism: a Full-Spectrum Characterization. *The AAPS Journal*. 2021;23. 9. Qian Y. The Potential for Pharmacokinetic Interactions Between Cannabis Products and Conventional Medications. *Journal of Clinical Psychopharmacology*. 2019;39(5):462-471. 10. Lynch T. The effect of cytochrome P450 metabolism on drug response, interactions, and adverse effects. *American Family Physician*. 2007;76(3):391-396. 11. FDA. Drug Development and Drug Interactions | Table of Substrates, Inhibitors and Inducers. Updated 08/24/2022. Accessed 09/08/2022, 2022.

This information is brought to you by Jazz Pharmaceuticals in partnership with the American College of the Apothecaries and Pharmacists Planning Services Inc.

**CANNABINOID  
CLINICAL**  
Visit [CannabinoidClinical.com](http://CannabinoidClinical.com)



©2022 Jazz Pharmaceuticals, Inc. All rights reserved. CCL-07080-1022



Refer to the **Medscape Drug Interaction Checker** as a resource for identifying potential drug interactions within patient-specific medication profiles.