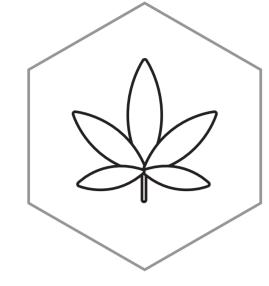
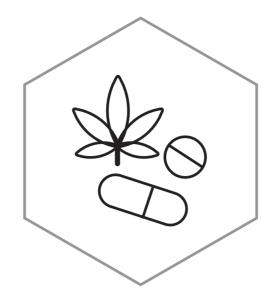
Some Things to Know When Using a Cannabis or Hemp Product



Cannabis and hemp products contain many active ingredients, such as **CBD**, **THC**, and others.



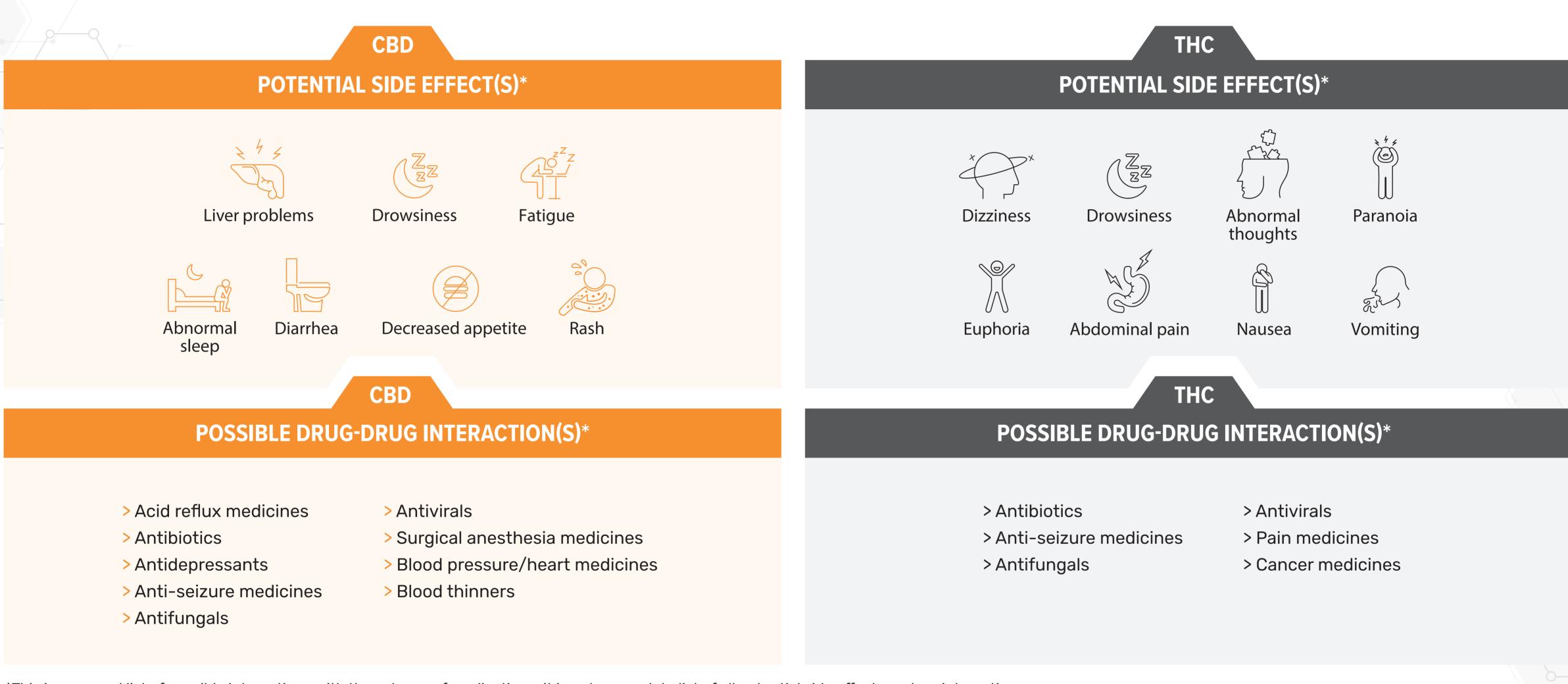
Both CBD and THC **can interact** with common medicines.



FDA approval requires assessment of benefits and risks of a product. FDA also inspects manufacturing.

If products do not go through an FDA review, it can be difficult to predict their interactions with other drugs. 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.



*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 48 warning letters to dispensary companies for incorrect labels and illegal advertising.[†]



A study of non-FDA approved products showed nearly 70% were mislabeled for CBD and another 20% contained undisclosed THC.*



FDA-approved products containing CBD and THC have undergone rigorous testing.

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

If you have additional questions, Greenwich Biosciences Medical Information department may be reached by email **medinfo@greenwichbiosciences.com** or by calling 1-833-424-6724.

[†]Based on warning letters sent from 2015 to September 2019. 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.

1. Syndros® [package insert]. Chandler, AZ: Insys Therapeutics, Inc.; 2018. **2.** Marinol® [package insert]. North Chicago, IL: AbbVie Inc.; 2017. **3.** Cesamet® [package insert]. Somerset, NJ: Media Pharmaceuticals Inc.; 2013. **4.** Epidiolex® [package insert]. Carlsbad, CA: Greenwich Biosciences, Inc.; 2018. **5.** United States Food and Drug Administration (FDA). FDA regulation of cannabis and cannabis-derived products: questions and answers. April 2, 2019. https://www.fda.gov/news-events/public-health-focus/fda-regulationcannabis-and-cannabis-derived-products-questions-and-answers#othercbdapproved. Accessed June 24, 2019. **6.** Cytochrome P450 Drug Interactions. Pharmacist Letter. May 2016. https://pharmacist.therapeuticreasearch.com/Content/Segment/PRL/2016/May/Cytochrome-P450-Drug-Interactions-9674. Accessed June 24, 2019.

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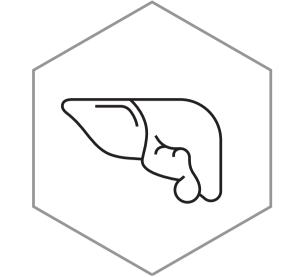








Importance of Monitoring Drug Interactions Between Your Patients' Medications and Cannabis Products



The cytochrome P-450 (CYP) system is one of the most important systems for drug metabolism



Approximately 60% of all clinically prescribed drugs are metabolized via CYP3A4



Cannabinoid products are cleared by the CYP-450 system, including CYP3A4

Cannabinoid products can be inducers or inhibitors of the various CYP enzymes; therefore, healthcare providers should consider monitoring patient's use of cannabis products to reduce the risk of adverse events and to maintain the effectiveness of other concomitant medications.

> Based on the 4 FDA-approved cannabinoid drugs, CBD and THC may have the following side effects and drug-drug interactions.

CANNABIDIOL (CBD)*

CBD is a substrate for CYP3A4 and CYP2C19. Therefore, drugs that inhibit or induce these 2 enzymes will affect the plasma concentration of CBD

CBD can function as an inhibitor, an inducer, or both

CBD	INHIBITION	INDUCTION
CYP1A2	+	+
CYP2B6	+	+
CYP2C8	+	
CYP2C9	+	
CYP2C19	++	
UGT1A9	+	
UGT2B7	+	

TETRAHYDROCANNABINOL (THC)*

THC is a substrate for CYP3A4 and CYP2C9. Therefore, drugs that inhibit or induce these 2 enzymes will affect the plasma concentration of THC

- THC is highly protein bound. May displace other drugs, increasing the risk of adverse events
- ✓ Added CNS effects (dizziness, sedation, confusion) when taken with **CNS** depressants
- Hypotension, hypertension, and tachycardia may occur when taken with drugs that also affect the cardiac system
- THC may lower seizure threshold. May affect anticonvulsants therapy

Potential drug interactions may occur with CBD and/or THC and the following medications:

- > Proton pump inhibitors
- > Antibiotics
- > Antidepressants
- > Anticonvulsants
- > Antifungals
- > Antivirals
- > Induction/anesthesia
- > Antihypertensives
- > Antipsychotics
- > Antiarrhythmics
- > Chemotherapy
 - > Opioids
 - > Sympathomimetics

> Benzodiazepines

- > Anticoagulants
- > Others

> Antiplatelets

Monitoring for safety and effectiveness is recommended.

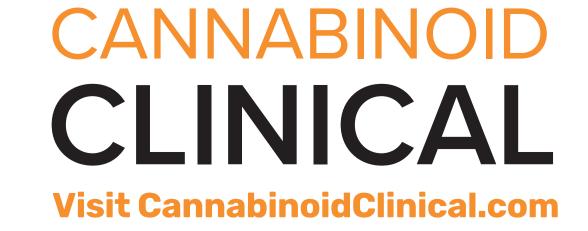
Advise patients to talk to their healthcare providers about their current medications and OTC products they are taking at their next visit.

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

If you have additional questions, Greenwich Biosciences Medical Information department may be reached by email medinfo@greenwichbiosciences.com or by calling 1-833-424-6724.

References: 1. Le J. Drug Metabolism. *Merck Manuals Professional* Edition. https://www.merckmanuals.com/professional/clinicalpharmacology/pharmacokinetics/drug-metabolism. Accessed August 23, 2019. 2. Iffland K, Grotenhermen F. An update on safety and side effects of cannabidiol: a review of clinical data and relevant animal studies. Cannabis Cannabinoid Res. 2017; 2(1):139-154. 3. EPIDIOLEX® [package insert]. Carlsbad, CA: Greenwich Biosciences, Inc.; 2018. 4. Marinol® [package insert]. North Chicago, IL: AbbVie Inc.; 2017. 5. Syndros® [package insert]. Chandler, AZ: Insys Therapeutics, Inc.; 2018. 6. Cesamet® [package insert]. Somerset, NJ: Media Pharmaceuticals Inc.; 2013.

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^{*}Not a complete list of all drug-drug interactions.