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

60%

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

CYP-450

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
- > Antiarrhythmics
- > Antipsychotics
- > Benzodiazepines
- > Chemotherapy
- > Opioids
- > Sympathomimetics
- > Anticoagulants
- > Antiplatelets
- > Others

Monitoring for safety and effectiveness is recommended.

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

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/clinical-pharmacology/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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