



Aetna Better Health® of New Jersey

# Cannabinoid Oil and Drug Interactions

## **Cannabis Plant:**

The Cannabis plant has roughly 100 known cannabinoids, the two primary being Tetrahydrocannabinol (THC) and Cannabidiol (CBD). THC is known for exerting psychoactive properties and is used as a measure of cannabis potency unlike CBD which does not carry psychoactive characteristics.

## **What is CBD Oil:**

Cannabidiol oil is extracted from cannabis flowers or leaves (usually from the C.Sativa variation) and dissolved in an edible oil. CBD oil may vary from “Hemp oil” which is usually derived from the seeds of C.Sativa (low to no THC levels) and “Cannabis oil” which carries the highest THC level and is derived from the more potent C.indica plant. Terminology, however, has become interchangeable and differentiation based upon THC levels is opaque. CBD oil can be administered orally or sublingually with dosing dependent on indication and patient response.

## **Is CBD Oil Legal:**

As of December 20, 2018 the Agriculture Improvement Act of 2018 was signed into law which redefined the legality of certain cannabis products. Hemp, defined as cannabis (*Cannabis sativa L.*) was removed from the Controlled Substance Act along with cannabis derivatives with extremely low (less than 0.3 percent on a dry weight basis) THC content, deeming these substances now legal under federal law.

## **Drug Interactions:**

The THC component of cannabis is primarily metabolized by the hepatic CYP-450 enzymes, CYP3A4 and CYP2C9, while CBD is metabolized by CYP3A4 and CYP2C19. Medications that process through these pathways have the potential to interact. Route of cannabis administration (i.e. inhaled vs oral) may affect extent of interaction.

# Cannabinoid Oil and Drug Interactions

Interaction Type*	THC	CBD
<b>Major Metabolic Pathway (CYP-450)</b>	CYP3A4 and CYP2C9	CYP3A4 and CYP2C19
<b>Affected Metabolic Enzymes/ Drug Transporters</b>	<ul style="list-style-type: none"> <li>• Potential to inhibit CYP2C8, CYP2C9, and CYP2C19</li> <li>• May induce or inhibit CYP1A2 and CYP2B6</li> <li>• Inhibits UGT1A9 and UGT2B7</li> </ul>	
<b>Potential Drug Interactions (CYP-450 Substrates)</b>	<ul style="list-style-type: none"> <li>• Anesthetics</li> <li>• Angiotension II blockers</li> <li>• Antiarrhythmics</li> <li>• Antibiotics</li> <li>• Antidepressants</li> <li>• Anti-epileptics</li> <li>• Antihistamines</li> <li>• Antipsychotics</li> <li>• Benzodiazepines</li> <li>• Beta blockers</li> <li>• Calcium channel blockers</li> <li>• HIV antivirals</li> <li>• HMG CoA reductase inhibitors</li> <li>• Immune modulators</li> <li>• NSAIDs</li> <li>• Oral hypoglycemic agents</li> <li>• PPIs</li> <li>• Sulfonylureas</li> <li>• Steroids</li> </ul>	
<p>*List is not comprehensive of all of the potential medications impacted by cannabidiol nor will each medication necessarily cause an interaction.</p>		

## References:

1. U.S. Food and Drug Administration. (2018). Statement from FDA Commissioner Scott Gottlieb, M.D., on signing of the Agriculture Improvement Act and the agency's regulation of products containing cannabis and cannabis-derived compounds. Retrieved from <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm628988.htm>
2. Gorelick, David A. (2018). Cannabis Use and Disorder. Hermann R, ed. UpToDate. Retrieved from <https://www.uptodate.com/contents/cannabis-use-and-disorder>
3. Natural Medicines Comprehensive Database Consumer Version [Internet]. Stockton (CA): Therapeutic Research Faculty; ©1995-Cannabidiol. Clove; [reviewed 2018 Oct 29; cited 2019 Jan 2]; Available from: <https://medlineplus.gov/druginfo/natural/1439.html>
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. URL: <http://www.clinicalpharmacology.com>. Updated August 2018.