

# First Script Prescription Benefit News for Workers' Compensation

March 2018

## Drug of the Month



### ZTildo™ (lidocaine topical system) 1.8%

A new prescription topical formulation of lidocaine was approved by the U.S. Food and Drug Administration (FDA) at the end of February. ZTildo (lidocaine topical system) 1.8% contains lidocaine in a topical patch form similar to currently-available Lidoderm® (lidocaine patch 5%).

Due to differences with ZTildo compared to Lidoderm in the proportion of drug that reaches circulation within the body, different dosage strengths are required to achieve equivalent results. The manufacturers of ZTildo, Scilex Pharmaceuticals, indicate that one ZTildo 1.8% patch provides equivalent lidocaine exposure to one Lidoderm 5% patch. The recommended dosing for ZTildo mirrors that of Lidoderm: up to three patches may be applied at a time once daily for up to 12 hours in a 24-hour period.

Also similar to Lidoderm, ZTildo is indicated for the relief of pain associated with post-herpetic neuralgia (PHN), a skin- and nerve-related condition resulting as a complication of shingles which is caused by the herpes zoster virus. Lidoderm is a commonly-prescribed medication in workers' compensation, although its use in workers' comp is primarily for "off-label" indications (i.e., those outside of the FDA-approved labeling for the drug). While ZTildo is not directly addressed today, the Official Disability Guidelines (ODG) support use of lidocaine patches on a trial basis if there is evidence of localized pain consistent with a neuropathic etiology, but only after a trial of first-line neuropathy medications (e.g., gabapentin, tricyclic or SNRI antidepressants). The recommended trial period is for no more than four weeks, during which ODG recommends no other changes to medication should be made, and outcomes for improvements in pain and function as well as any decreased need for use of other medications should be assessed.

References:  
<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/>

## Regulatory Update



### Pennsylvania

On February 6, 2018, the Pennsylvania Senate's proposed drug formulary for the State of Pennsylvania failed to pass in the House.

On October 20, 2017, the State of Pennsylvania introduced [Senate Bill 936](#). The bill would have amended the state's Workers' Compensation Act to require the Department of Labor to adopt an evidence-based prescription drug formulary, and require Utilization Review Organizations (UROs) and Peer Review Organizations (PROs) be accredited by a nationally recognized organization selected by the Department of Labor.

### Indiana

On February 6, 2018, the Indiana Senate passed [SB 369](#), the state's first workers' compensation specific drug formulary. The bill was also passed by the House on March 13, 2018, and is now with Governor Eric Holcomb awaiting his signature.

Coventry's Regulatory and Legislative Affairs (RLA) group will continue to monitor further discussion on these topics. If you have questions regarding this decision, please contact your First Script Account Manager.



## Ask The Pharmacist

To suggest a topic, send an email to: [AskThePharmacist@cvtv.us.com](mailto:AskThePharmacist@cvtv.us.com)

# Can marijuana, medicinal or otherwise, affect the other medications a person is taking?

The changing regulatory landscape surrounding marijuana, also referred to as “cannabis,” can certainly be expected to have some impact on the frequency with which we may encounter patients who are using some form of the drug. Regardless, cannabis should be approached much like any other substance or medication a patient takes, with full consideration given to potential drug interactions, side effects, dosing decisions, and general patient safety concerns. For the purposes of the question posed here, we focus on some of the potential drug-drug interactions associated with cannabis.

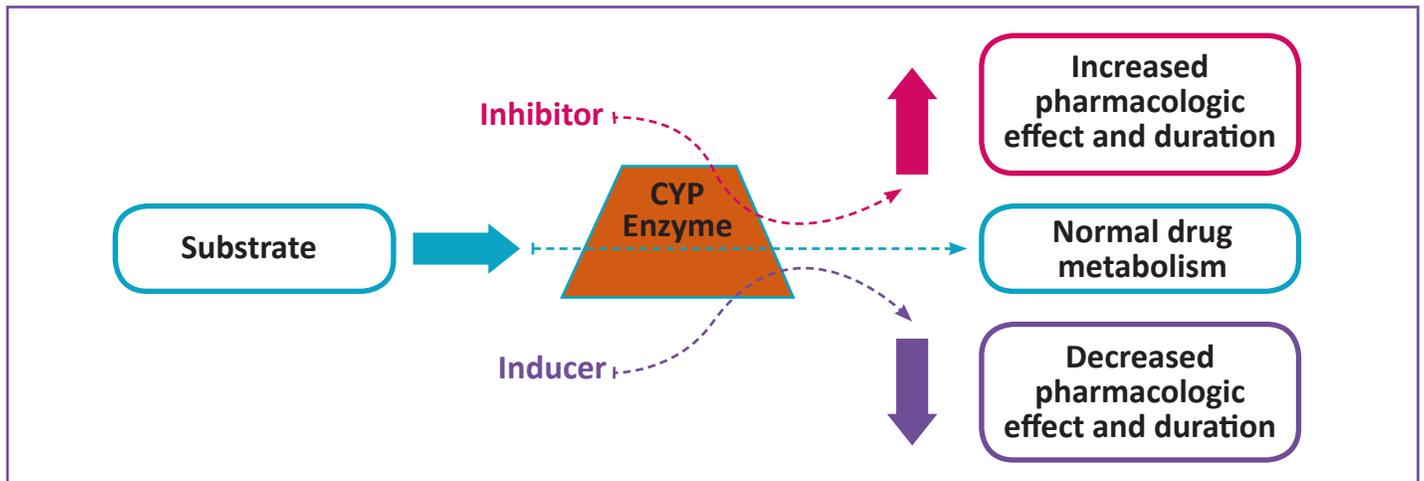
In order to understand how cannabis may affect other drugs a person may be taking (and vice versa), it is helpful to distinguish some of the components of cannabis that determine potency and effects, also known as “cannabinoids.” Today, the two cannabinoids of the most therapeutic interest are **Δ9-tetrahydrocannabinol (THC)** and **cannabidiol (CBD)**. These cannabinoids interact with the cytochrome P450 (CYP) enzyme system, one of the main pathways through which drugs are broken down, or “metabolized,” by the body.<sup>1</sup>

Many other drugs affect or use this CYP450 system, and thus may alter the therapeutic effect, duration, and side effects of another drug.

- Drugs that are metabolized by the CYP450 system are categorized as “**substrates**”
- Drugs that affect CYP enzymes to decrease their ability to breakdown a drug are called “**inhibitors**”
- Drugs that affect CYP enzymes to increase CYP enzyme activity and metabolism of a drug are called “**inducers**”

This becomes important because more or less of a substrate drug may then be present in the body than expected.<sup>2</sup>

### CYP450 Enzyme Drug Metabolism Inhibition and Induction



Not a lot of research is available on all of the possible or known drug-drug interactions related to cannabis due to the challenges surrounding clinical studies of a drug that is still classified as illegal at the federal level (marijuana is a Schedule I controlled substance). However, we do have evidence documenting some of the observed interactions, which allows us to apply predictions based on what we know about how cannabinoids may interact with the CYP450 system. Studies have shown that THC and CBD inhibition and induction at major CYP450 enzymes “**generally reflect a low risk of clinically significant drug interactions with most use, but specific human data are lacking.**”<sup>1</sup>

### Drugs that may increase cannabinoid effects

Known inhibitors of the CYP enzymes involved in THC and CBD metabolism include:

- Several anti-infective agents (e.g., fluconazole, ketoconazole, clarithromycin)
- The opioid-containing drug Suboxone® (buprenorphine and naloxone) indicated for the treatment of opioid dependence
- PPIs (e.g., omeprazole, esomeprazole, lansoprazole, pantoprazole)

Thus, if a patient is taking one of these medications while using a product with THC or CBD, there is a potential for increased cannabinoid effects.

*(Continued on page 3)*

## Drugs that may decrease cannabinoid effects

Known inducers of the CYP enzymes involved in THC and CBD metabolism include:

- A handful of anticonvulsants (e.g., carbamazepine, oxcarbazepine, phenytoin)
- Steroids (e.g., prednisone, glucocorticoids)

If a patient is taking one of these inducers while using a product containing THC or CBD, there is a potential for decreased cannabinoid effects. Interestingly, research has shown significant antagonistic (blocking or decreasing effect) interactions with CBD and clobazam or carbamazepine, all three of which can be used for seizure disorders in select patients.<sup>3</sup>

Also of note, CBD itself is a powerful inhibitor of certain CYP enzymes, thus it may increase the pharmacologic effects of:

- Some opioids (e.g., oxycodone, tramadol)
- Antibiotics
- Calcium channel blockers
- Antidepressants
- Antihistamines

## Drugs with clinically important drug-drug interactions with marijuana

When drugs with particularly sensitive dosing considerations, such as the anticoagulant warfarin, also use the same enzyme pathways as THC or CBD, special attention is warranted to monitor for the possibility of an enhanced anticoagulant effect and an increased risk of bleeding through drug-drug interactions. Tricyclic antidepressants such as amitriptyline are often prescribed in the injured worker population for chronic pain, and these drugs also use common CYP enzyme pathways. Observed tricyclic antidepressant interactions with THC and CBD have shown possible temporary cognitive changes, delirium, or abnormally rapid heart rate as well as possible increased THC effects with concurrent use.

The Colorado Department of Public Health and Environment put forth the following list of drugs for which reliable evidence supports the presence of clinically important marijuana-related drug-drug interactions.<sup>4</sup>

chlorpromazine	hexobarbital	clobazam	protease inhibitors (indinavir, nelfinavir)		
hydrocortisone	theophylline	clozapine	ketoconazole	tricyclic	antidepressants
CNS depressants	MAO inhibitors	warfarin	disulfuram	phenytoin	

## Combined effects of sedatives and cannabis

Beyond the potential for drug interactions through effects on drug metabolism, cannabis can intensify certain effects of other drugs through a synergistic or additive nature. For example, cannabis is a CNS depressant and can result in a slowing down effect of functions related to the central nervous system (i.e., breathing rate, heart rate, consciousness). If cannabis is used with other CNS depressants, such as alcohol, opioids, benzodiazepines and the like, the sedative effects can be greater than if the substance(s) are used alone.

It is clear that more research is needed to better identify interactions between cannabis and prescription drugs. However, cannabis may have a role in a variety of medical conditions when patients have failed other FDA-approved treatments, and the reality is that cannabinoids are becoming more widely used as more and more states are adopting regulations supporting their use. As with any treatment, adverse effects and drug interactions do occur, so benefits and risks should always be weighed for each individual while considering overall patient safety and public health concerns. For further insight into drug-drug interactions or for questions related to a specific injured worker's care, please consider contacting our team of clinical pharmacists at [askthepharmacist@cvty.com](mailto:askthepharmacist@cvty.com).

### References:

1. Stephen M. Stout & Nina M. Cimino (2013). Exogenous cannabinoids as substrates, inhibitors, and inducers of human drug metabolizing enzymes: a systematic review. *Drug Metabolism Reviews*, 46:1, 86-95. Available at: <https://doi.org/10.3109/03602532.2013.849268>. Accessed: March 5, 2018.
2. Flockhart Table, P450 Drug Interaction Table. Available at: <http://medicine.iupui.edu/clinpharm/ddis/main-table/>. Accessed: March 5, 2018.
3. American Epilepsy Society Annual Meeting December 2015
4. Colorado Department of Public Health and Environment. Monitoring Health Concerns Related to Marijuana in Colorado. 2016. Available at: <https://www.colorado.gov/cdphe/marijuana-health-report>. Accessed: March 8, 2018.

# Clinical Controls Now Applied to Combo Pack Kits

First Script is now applying clinical controls to identify and block the dispensing of prescriptions for fixed combination and co-packaged drugs, often referred to as Combo Pack Kits.

## What is a Combo Pack Kit?

Combo Pack Kits consist of multiple products that are conveniently packaged together for sale. The kits can contain combinations of over-the-counter (OTC) medications, prescription medications, and/or medical devices and supplies. These packaged products can be used at the same time or independently at different times for a common therapeutic purpose. Manufacturers also promote Combo Pack Kits as value packs, convenient packs, family packs, or multi-unit variety packs.

A few common examples include:

- Local anesthetics with an added moisturizing cream
- Pre-filled drug delivery systems
- Topical analgesic medical supplies

## How are Combo Pack Kits identified?

The identification of Combo Pack Kits remains elusive, as the manufacturer is able to obtain a unique, single National Drug Code (NDC) for each multi-ingredient kit, vs. each individual item. By doing so, manufacturers are able to charge more for the kits under the assumption the multi-ingredient product more closely meets the needs of the condition.

## Why should Combo Pack Kits be blocked?

Combo Pack Kits are often sold at a much higher rate than when packaged individually. Frequently, all the components of the Combo Pack Kit are not medically necessary, and offer little or no added value beyond what the same individually prescribed items would provide. In cases where the combined products are medically necessary, there is typically a cost savings achieved when necessary items are prescribed and dispensed individually.

## What is First Script doing to address Combo Pack Kits?

First Script pharmacists are able to identify Combo Pack Kits, and have rules in place to block the dispensing of these kits without prior authorization. We have also added a new Smart Prior Authorization message to our online tool, Coventry Connect, to alert claims examiners to the new recommendations which states:

“Recommend denial – This product is a combination drug kit that has two or more products packaged together for the user’s convenience. It combines over-the-counter medications, prescription medications, and/or medical devices and is sold at a much higher cost than when these products are sold individually. Additionally, some of the ingredients may not be necessary for the injured worker. If medically necessary, recommend approval for alternative therapies that are commercially available as individual drug/agent.”

For more information on the use of Combo Pack Kits, please contact your Account Manager or Account Pharmacist.

---

*The information which is provided herein is offered as a courtesy to our clients. All material is intended for information, communication and educational purposes only and is in no manner an endorsement, recommendation or approval of any information. Coventry accepts no liability for the content of this distribution, or for the consequences of any actions taken on the basis of the information provided.*

---