

# Long-Term Care Updates

March 2019

## Should elderly patients join the CBD bandwagon?

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### Introduction:

Cannabidiol (CBD) is a constituent derived from cannabis plants. Unlike delta-9-tetrahydrocannabinol (THC), CBD is not psychoactive. This means that CBD does not produce the same euphoric, “high” feeling that users of THC-containing products report.<sup>1</sup> The use of CBD products has gained popularity in the last few years as CBD products have become more readily available and anecdotal reports, laboratory research, and some clinical research have suggested the potential for some therapeutic benefits associated with this compound. Still, research on the safe and effective use of CBD, particularly in the elderly population, is limited. Pharmacists and other healthcare providers are commonly faced with questions on the legality and appropriate use of CBD products. The following article will review the legal status of CBD, its clinical effects in elderly patients, and safety concerns associated with its use.

### Legality:

The most recent Farm Bill, passed by Congress in December 2018, provided some clarification on the legality of CBD-based products. An excerpt from a Brookings Institution article on the Farm Bill follows:<sup>2</sup>

“[S]ection 12619 of the Farm Bill removes hemp-derived products from its Schedule I status under the Controlled Substances Act, but the legislation does not legalize CBD generally. ...CBD generally remains a Schedule I substance under federal law. The Farm Bill—and an unrelated, recent action by the Department of Justice—creates exceptions to this Schedule I status in certain situations. The Farm Bill ensures that any cannabinoid—a set of chemical compounds found in the cannabis plant—that is derived from hemp will be legal, *if and only if* that hemp is produced in a manner consistent with the Farm Bill, associated federal regulations, association state regulations, and by a licensed grower. All other cannabinoids, produced in any other setting, remain a Schedule I substance under federal law and are thus illegal. (The one exception is pharmaceutical-grade CBD products that have been approved by FDA, which currently includes one drug: GW Pharmaceutical’s Epidiolex.)”

However, while the Farm Bill makes clear that hemp-derived CBD is now legal to produce, the story doesn’t end there. The US Food, Drug, and Cosmetics Act makes it illegal to introduce drug products into dietary supplements. Because CBD is now an ingredient in an FDA-approved prescription drug (Epidiolex), it is no longer considered a dietary supplement. Thus, according to the FDA, CBD is not considered a legal dietary supplement, even if it is derived from hemp.<sup>3,4</sup> That said, CBD products continue to show up on the shelves of convenience stores, natural health markets, and specialty retail stores. This puts pharmacists who want to practice within the scope of the law but also appropriately counsel patients in a difficult position. For now, pharmacists should avoid recommending over-the-counter CBD products while still providing patients who choose to use CBD with information on potential safety concerns associated with its use.

## Clinical Efficacy:

Some animal and in vitro research suggests that CBD has certain pharmacologic effects that may make it a candidate for treating depression, pain, inflammation, anxiety, insomnia, and neurodegenerative disorders, among other uses. Additionally, a few clinical trials and case reports have documented positive outcomes related to the use of CBD in patients with anxiety, bipolar disorder, epilepsy, insomnia, and schizophrenia. However, patients in these studies were younger and without significant comorbidities.<sup>3</sup>

To date, clinical research on the use of CBD in elderly patients is limited to those with Parkinson's disease. A review of this research follows:

In 2009, Zuardi et al. published results from an open-label pilot study assessing the safety and efficacy of CBD in six patients with Parkinson's disease, specifically those with symptoms of psychosis. CBD was given at an initial dose of 150 mg daily and titrated up by 150 mg weekly based on clinical response and tolerability for a total of 4 weeks. The researchers reported significant improvements in the Unified Parkinson's Disease Rating Scale (UPDRS) total score, Brief Psychiatric Rating Scale (BPRS) total score, and Clinical Global Impression of Improvement (CGI-I) score compared to baseline. No adverse events related to CBD use were reported.<sup>5</sup>

In 2014, Chagas et al. published results from a randomized, double-blind, placebo-controlled trial assessing the safety and efficacy of CBD in 21 patients with Parkinson's disease. Patients, ranging in age from 51 to 82 years without comorbid psychiatric disorders, were randomized to receive CBD 75 mg, CBD 300 mg, or placebo daily for 6 weeks. No significant improvement in UPDRS was reported with either dose of CBD. However, the higher CBD dose was found to significantly improve total well-being and quality of life scores, assessed by the Parkinson's Disease Questionnaire-39 (PDQ-39), compared to placebo. No significant adverse effects were reported in patients taking CBD.<sup>6</sup>

Both studies describe some positive findings but are not without limitations. The first study, by Zuardi et al., has a very high risk for bias due to the very small sample size, lack of placebo-control, and lack of blinding. The more recent study by Chagas et al. is of higher quality, although it's unclear whether these results will apply to the broader population of Parkinson's patients due to the small number of subjects studied. Additionally, because the studies lasted for only 4-6 weeks, the long-term safety and efficacy of CBD in Parkinson's patients is unknown.

## Safety:

### Adverse effects:

There is limited evidence on the incidence of adverse effects in elderly patients taking CBD products.<sup>1</sup> However, the trials summarized above suggest that CBD at doses up to 300 mg daily for up to 6 weeks is well tolerated.<sup>4,5</sup> A number of adverse effects in clinical studies of younger patients taking CBD have been identified, some of which would be more problematic if experienced in elderly patients.<sup>1</sup>

Potential adverse effects of concern in elderly patients taking CBD include sedation, psychomotor slowing, orthostatic hypotension, and lightheadedness. These adverse effects could potentially increase the risk of falls in older adults. Gastrointestinal adverse effects such as dry mouth, decreased appetite, and weight loss have also been reported in some patients taking CBD and could be particularly bothersome in elderly patients. These side effects tend to be worse with doses above 15-20 mg/kg per day.<sup>1</sup>

### Drug-interactions:

A number of potential drug-interactions with CBD have been identified in clinical and laboratory studies. These interactions are summarized in the table on the next page.

Table. Potential drug-interactions with CBD<sup>1,7</sup>

Drug/Class of Concern	Comments
Antiepileptic Drugs	<ul style="list-style-type: none"><li>● Clinical research shows that CBD at doses ranging from 5-50 mg/kg daily can significantly increase drug levels of concomitantly administered antiepileptic medications, including clobazam, eslicarbazepine, rufinamide, topiramate, and zonisamide.</li><li>● These interactions are likely due to inhibition of the CYP isoenzymes involved in the metabolism of these drugs.</li><li>● If concomitant use of CBD with these drugs cannot be avoided, drug levels should be monitored more closely.</li><li>● Concomitant use of CBD with valproic acid has been reported to increase liver function tests. Liver function should be monitored more closely in patients taking CBD and valproic acid.</li></ul>
CNS Depressants	<ul style="list-style-type: none"><li>● High dose CBD may be associated with sedative and hypnotic effects.</li><li>● Combining CBD with CNS depressants could theoretically lead to additive sedations.</li><li>● This interaction is theoretical in nature and has not been documented in humans.</li></ul>
CYP Substrates (1A1, 1A2, 1B1, 2A6, 2B6, 2C19, 2C9, 2D6, 3A4)	<ul style="list-style-type: none"><li>● Laboratory studies suggest that CBD inhibits a number of CYP isoenzymes, theoretically increasing the risk of adverse effects in people taking drugs that are metabolized by these isoenzymes.</li><li>● Patients taking CBD products along with drugs metabolized by these isoenzymes should be monitored more closely for adverse effects.</li><li>● Interactions between CBD and drugs metabolized by CYP2C19 or CYP3A4 have been documented in human studies, suggesting that these combinations be avoided, if possible, or monitored more closely.</li></ul>

### Conclusion:

CBD is currently illegal in the eyes of the FDA. However, CBD products are still available for purchase at many retail locations and online stores. It's possible the legal status of CBD products could change as the FDA continues to evaluate the safety of these products. Until then, given the illegality of CBD and paucity of long-term safety and efficacy data regarding its use in elderly patients, pharmacists should avoid recommending CBD products in this population. Older adults who choose to take CBD should be counseled on the potential for adverse effects, screened for potential drug-interactions, and encouraged to report the use of CBD to their healthcare providers.

## References:

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