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# Safety considerations for patients using cannabis

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## Abstract

Cannabis is the most used federally illicit substance in the United States, yet there is limited knowledge about its pharmacology; efficacy for various medical conditions; or, more importantly, its safety profile. There is significant interest in exploring the full extent of the pharmacologic effects of cannabinoids. Psychoactive effects of cannabis are well-established, but the other effects of cannabinoids, including their effect on mood symptoms; suicidal ideation; and activity outside of the central nervous system, including actions on the cardiovascular system, are still being uncovered. With an increasing number of states in the United States independently authorizing medicinal and, in some cases, recreational use of cannabis, it is essential that our health care professionals are aware of these potential risks when caring for patients who are using cannabis. The objective of this manuscript is to describe how mood symptoms, suicidality, cardiovascular effects, and drug interactions may be associated with cannabis use.

**Keywords:** cannabis, adverse effects, suicidality, cardiovascular effects, drug interactions

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## Introduction

Cannabis is reported to be one of the most frequently used substances in the United States.[1] In this paper, the term "cannabis" is used to refer to plant material and products derived from the *Cannabaceae* family, which contain chemical compounds called cannabinoids.[2] Two main cannabinoids found in cannabis are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD).[2] According to the 2022 National Survey on Drug Use and Health (NSDUH), 61.9 million (22%) individuals 12 years of age or older reported use of cannabis in the last year with 42.3 million (15%) reporting use in the past month.[1] Respondents 18 to 25 years old had the highest usage rates at 38.2%, followed by individuals 26 years or older at 20.6%, and those 12 to 17 years of age at 11.5%.[1] This places cannabis as the third most popular substance used by those 12 years of age or older after alcohol and tobacco products in the United States.[1] Factors contributing to the rise in popularity of cannabis likely include the expanding availability of cannabinoid products and medicinal cannabis, legalization of recreational cannabis in select states, and the diversification of cannabis formulations.

The potency of THC in cannabis products has risen significantly over the last few decades. The National Institute on Drug Abuse and the University of Mississippi analyzed cannabis plant material and found the average THC concentration rose from 3.4% in the early 1990s to 10% by 2010, continuing up to 16% in 2022.[2,3] Cannabis products such as hashish and hash oil were found to have THC concentrations of more than 20% with hash oil having a peak potency of 31%.[3] CBD concentrations over this same

### Take Home Points:

- Cannabis use is associated with increased depression symptoms in individuals consistently using cannabis, including those with cannabis use disorder and adolescents and young adults. The presence of cannabis in individuals who present for suicidal ideation and in those who completed suicide suggest this may be a risk factor especially in younger patients and those using other substances such as alcohol. Proactive screening for cannabis use disorder and depression symptoms may help identify at-risk patients before they find themselves in a crisis.
- Cardiovascular changes associated with cannabis use include tachycardia, blood pressure fluctuations, and an increased risk of myocardial infarction or ischemic strokes in high-risk populations. Integrated mental and physical health care coordination may identify individuals at risk by allowing focused treatment and monitoring to prevent cardiac events.
- Cannabinoids are metabolized by the cytochrome P450 enzymes; some also serve as inhibitors of several enzymes, making them susceptible to pharmacokinetic drug interactions. The diverse pharmacodynamic effects of cannabinoids also introduce the possibility of pharmacodynamic interactions with various medications such as enhanced sedation with central nervous system depressants.

time frame have not significant changed.[2] Rising potency of cannabis products should raise concerns regarding the safety of cannabis products; this has not been the case as discussions related to cannabis safety, misuse, and cannabis use disorder (CUD) have been limited. Estimates suggest that between 10% and 30% of individuals who use cannabis meet criteria for CUD.[4,5] The United Nations 2022 prevalence data on cannabis use estimates approximately 22 to 68 million patients meet CUD criteria worldwide, with 6 to 18.5 million patients in the United States.[1,4-6] The NSDUH survey found consistent numbers with 19 million respondents 12 years of age or older reporting CUD in the past year with 55.1% classified as a mild disorder and 17.3% as severe CUD.[1] Patients with CUD were more likely to have an alcohol use disorder with an odds ratio (OR) of 6.0; another drug use disorder (OR 9.0); or a mental health disorder, including personality disorder (OR 4.8), posttraumatic stress disorder (OR 4.3), mood disorder (OR 3.8), and other anxiety conditions (OR 2.8).[5]

The US Preventive Services Task Force recommends screening adolescents 12 to 17 years of age and adults 18 years or older about drug use, including cannabis use, in primary care settings when services and care can be offered or a referral provided.[7] Specific tools that screen for CUD include: the 4-question screening (CAGE-cannabis), the Cannabis Abuse Screening Test, the Cannabis Use Disorders Identification Test-Revised, the Cannabis Use Problems Identification Test, Severity of Dependence Scale, and the Single-Item Screen-Cannabis.[8-13] Each tool is self-reported and targets adolescents and adult respondents with score cutoffs to identify the threshold for problematic cannabis use.[8-13] Selection of the screening tool is population- and health care setting–dependent. Broad implementation of 1 screening tool to identify patients with CUD is a first step toward determining factors that increase the risk for CUD and can help identify future risk factors for CUD. Currently, few risk factors for CUD have been identified. However, individuals who used cannabis daily or weekly for a year and those who began using cannabis before age 16 were more likely to develop CUD.[5]

Despite the uncertainty about adverse effects or long-term outcomes of CUD, the public does not appear troubled by the lack of safety information. A national survey of 979 participants found that 49.6% of respondents agreed that legalization of cannabis would result in increased cannabis access by youth, leading to increased long-term health risks, and only 39.8% agreed that cannabis legalization would increase health care spending due to direct and indirect effects of cannabis use.[14] Safety concerns with cannabis have been identified, including the dose-related risk of cannabis use and psychosis[15-17] and increased respiratory complications in those who smoke cannabis.[18] Without any expectations or pressure from the public to evaluate the safety of cannabis or the risks of CUD, it is essential that health care professionals remain well-informed on the risks identified with cannabis use. This knowledge will prepare them to optimize the care for patients who use cannabis, especially those with CUD. The objective of this paper is to use hypothetical case scenarios to describe evidence of increases in mood symptoms and suicidality along with cardiovascular concerns and drug interactions associated with cannabis use.

## Case 1

A 21-year-old patient with a history of major depressive disorder (MDD) and CUD is brought to an outpatient crisis center for evaluation. The patient reports using cannabis once weekly until it became available recreationally 3 months earlier when the patient's use increased to twice daily. Evaluation of the patient at the crisis center found that the patient had a Beck Depression Inventory (BDI) score of 29; the prior BDI score was from the patient's last clinic visit 3 years ago, and the score was 5. The patient reports no regular psychiatry appointments over the last 3 years as depression symptoms had

been controlled. The patient has a flat affect; reports decreased interest, motivation, or pleasure in any activities; denies any symptoms of psychosis; and admits to feeling hopeless. These symptoms seemed to have started within the last month. When directly questioned, the patient endorses suicidal thoughts with a plan of overdosing on prescription and over-the-counter medication.

The relationship between cannabis use and affective disorders, including depression, is not as clearly described as the relationship between cannabis and psychosis.[15-17,19] Whereas psychosis tends to be seen following cannabis use in a dose-dependent manner,[15-17,19] depressive symptoms have been reported both preceding and following cannabis use.[20] The patient in Case 1 did not experience the psychotic symptoms despite the increase in cannabis use but has experienced worsening depressive symptoms. The National Epidemiologic Survey on Alcohol and Related Conditions data for individuals 18 years of age or older found that lifetime CUD and past year CUD were both associated with an increased risk of being diagnosed with MDD in the past year with an OR of 2.8 (95% confidence interval [CI] 2.33-3.41) for lifetime cannabis use and OR 2.6 (95% CI 2.26-2.95) for past year use cannabis use.[21] A systematic review exploring the effect of cannabis use on depressive symptoms found an increased rate of depression in adolescents and young adults up to 32 years old who use cannabis compared with individuals that did not use cannabis with an OR of 1.37 (95% CI 1.16-1.62).[22]

The US Preventive Services Task Force recommends screening for depression in all adults, including pregnant, postpartum, and older adults.[23] Depression screenings tools such as the Patient Health Questionnaire, the Center for Epidemiologic Studies Depression Scale, BDI, the Well-Being Index, or the Geriatric Depression Scale may be incorporated into electronic medical record platforms to ensure the data is captured and can be monitored for trends in depression symptoms.[23-28] Incorporating depression screenings into primary care settings can expand the monitoring, resulting in prospective identification of patients who could benefit from early intervention. Early identification may reduce time from symptom onset to initiation of treatment interventions such as motivational interviewing and cognitive behavioral therapy. Nonpharmacologic approaches may be more beneficial than pharmacologic treatment as initial trials with fluoxetine, venlafaxine, and quetiapine have not demonstrated effectiveness for treating depression in patients with CUD.[23,29-35] Depression screens in all adults is strongly encouraged; however, targeting cohorts at higher risk for depression with cannabis use, such as younger patients or those with an existing substance use disorder, would be an appropriate initial step prior to scaling to screen all adults.[22,23]

Determining the role of cannabis in this suicidality can be tricky. Suicidality includes suicidal ideation, suicide attempts, and/or general suicide behavior. Studies attempting to define the association between cannabis use and suicidality have been constrained by confounders. Difficulty quantifying the dose or frequency of cannabis, establishing the time frame of suicidal ideation in relation to cannabis use, and the complexities introduced with concomitant substance use and comorbid conditions have all been recognized as confounders. Estimates of suicidality in individuals who are using cannabis vary by cohort. A comparison of those who use cannabis with non–cannabis users from the general population found cannabis users that have epilepsy did not have an elevated suicidal ideation risk with an OR of 0.75 (95% CI 0.35-1.60) or suicide attempt risk OR 0.75 (95% CI 0.30-1.87).[36] Individuals who were daily or near daily cannabis users did have an elevated suicidality risk compared to non–cannabis users with an OR of 3.2 (95% CI 1.72-5.94), and adolescents also carried a higher risk of suicide attempt with an OR of 3.46 (95% CI 1.53-7.84).[22,37,38] Coroner toxicology results from individuals who died by suicide found cannabis present in an average of 9.5% of suicides.[38] Similar findings were seen in an evaluation of more than 1400 autopsy reports in individuals 15 to 60 years old who died by suicide but did not overdose; cannabis was found to be the most common illicit substance detected in 10.5% of cases.[39] It was found that the rates of those who died by suicide were higher for younger patients and those with a substance use disorder.[38,40,41] In individuals who died by suicide whose age was up to 24 years old, 27.3% tested positive for cannabis, and 27% of individuals with a drug use history who died by suicide were positive for cannabis.[38] The patient in Case 1 is 21 years old, which appears to increase the risk for suicidality, further supporting the need for evaluation and close monitoring of the patient.

It could be argued that cannabis was an anecdotal finding in those who died by suicide and that exploring the role of cannabis in those who attempt suicide or those with suicidal ideation would be more informative. A study evaluating self-reported cannabis use prior to a suicide attempt found that 10.2% of those who recently attempted suicide used cannabis within 24 hours of the attempt, and 13.2% used cannabis the day before the attempt.[38] Drug Abuse Warning Network data from 2011, which included 228 366 emergency department visits of suicide attempts that involved medications found cannabis present in 15 615 (6.8%), and 45.7% of these individuals also had alcohol present.[42] A meta-analysis evaluating 25 clinical trials investigating cannabis use and suicidal ideation or behavior found an OR of 3.2 (95% CI 1.72-5.94) for daily or near daily use, classified as heavy cannabis use, and suicide attempts compared with the general population and that those with psychotic and affective disorders using cannabis were 2.6 and 1.7 times, respectively, more likely to attempt suicide.[37,38] This evidence suggests that patient 1's increased frequency of cannabis use may have been a contributing factor in the current suicidal ideation the patient is experiencing.

The US Preventive Services Task Force does not recommend universal screening for suicide due to inadequate evidence.[23] Whereas universal screenings are not recommended, screenings for patients with depressive signs and symptoms such as the patient in Case 1 are necessary. In this case, it was fortunate that the patient presented for help prior to acting on these suicidal thoughts. Clear messaging on how to access services may help enhance patient awareness of when and how to reach out for services should patients experience suicidal thoughts. Efforts such as advertising the suicide prevention hotline or the crisis text line along with signs about symptoms of suicidal behavior in public areas of health care centers is a suitable place to start. Additionally, educating the public at health events and encouraging health care professionals to consider screening high-risk populations, such as those using alcohol or patients with psychotic or affective disorders, for suicidality would be reasonable pilot cohorts.[37,42] Establishing a library of resources and interprofessional partners, including crisis centers and medical and psychiatric care, can streamline care if patients are expressing suicidal thoughts in primary care settings, which are not always designed for this type of triage. Proactive implementation of these features creates a robust safety net for at-risk individuals.

## Case 2

A 69-year-old patient calls the community mental health center's triage hotline complaining of severe chest pain, sweating, and shortness of breath. The patient has hypertension, hyperlipidemia, obesity, a prior myocardial infarction (MI) in 2002, schizoaffective disorder, and suspected CUD. After several years of abstinence from cannabis, a neighbor moved into the building a month earlier, and this individual is routinely using cannabis. The patient admits to joining the neighbor several times daily to smoke cannabis. Over the past week, the patient reports having felt short of breath when leaving the neighbor's apartment and developing chest pain while walking the short distance back to the patient's own apartment. Today these symptoms progressed in severity with the patient reporting breaking out in a sweat, having a sense of doom, and becoming too weak to walk back to the apartment and called for help.

Cannabis use has infrequently been associated with cardiovascular events.[43] The cannabinoid receptor 1 (CB1), a main site of action for THC, can be found on heart and vascular smooth muscle.[44,45] Activation of CB1 receptors in vitro has resulted in activation of the mitogen active protein kinase pathway, and this may interfere with normal vasodilation, increase reactive oxygen species, enhance proliferation of vascular smooth muscle, and promote cholesterol production.[43] All of these actions can contribute to endothelial dysfunction and the development of atherosclerosis, which may ultimately lead to a cardiovascular event.[43]

In vitro pharmacologic actions do not always clearly translate into clinical effects. Clinically, cannabis has been observed to increase heart rate with changes ranging from 20% to 100% change from baseline that lasts for 2 to 3 hours.[43,46-48] Changes in blood pressure have also been reported with alterations ranging from no apparent change in blood pressure to individuals experiencing hypotension and hypertension.[44,46-48] These changes may not appear clinically significant alone, but in patients with preexisting conditions, they may contribute to the risk of developing a significant cardiac event. In a small study of patients with chronic, stable angina, exposure to 1 cannabis cigarette resulted in a decrease in time from exercise onset to angina by 50%.[45] In addition to causing angina, a meta-analysis of 36 studies evaluating MI triggers ranked smoking cannabis as the third most common MI trigger after use of cocaine and heavy metal exposure.[49] The effects of cannabis on cardiac tissue may be time-dependent as a multicentered study of 3882 patients presenting with an MI found an increased risk of MI within the first hour after cannabis inhalation compared with a period of not inhaling cannabis with a relative risk (RR) of 4.8 (95% CI 2.9-9.5).[50] In the second hour after cannabis use, the risk reduced to RR 1.7 (95% CI 0.6-5.1).[50] A retrospective analysis of 2097 patients followed for 11.2 years found cannabis use associated with increased all-cause mortality with a hazard ratio (HR) 2.09 (95% CI 1.25-3.5) and cardiovascular death HR 2.13 (95% CI 1.03-4.42).[45] Additionally, a study evaluating the National Inpatient Sample of patients 15 to 54 years old from 2004 to 2011 found the RR of ischemic stroke in cannabis users compared to nonusers to range from 1.45 (95% CI 1.42-1.49) to 2.26 (95% CI 2.14-2.38) with those aged 45 to 54 years with the lowest risk and those 25 to 34 years with the highest risk.[49]

Patients may feel more comfortable reaching out to their psychiatric providers even with medical concerns. To accommodate this, interprofessional integrated care teams can address medical conditions in psychiatric settings in which patients are most comfortable. Psychiatric medications may contribute to the development of medical conditions; routine screening of weight, vital signs, and laboratory results may identify those patients at risk for cardiac events. Patients with hypertension and elevated low-density lipoproteins and tobacco and cannabis smokers may benefit from close follow-up and treatment to reduce cardiac events.[45,50-53] Cardiovascular risk has been identified primarily with users who smoke cannabis; it is unclear at this time if the same risk is seen in patients who use different routes of administration, such as topically or oral ingestion. This risk should not be discounted, however, as the NSDUH survey found that 78.4% of cannabis users were smoking cannabis, and it was the most popular route of administration.[1] Future research evaluating new cannabis formulations and different routes of administration would be quite valuable in defining cannabis's effect on high-risk cardiovascular disease patients. Based on the existing information, there is an increased risk of cardiac events in high-risk patients;

therefore, providing educational materials, such as signs of cardiac symptoms (ie, chest pain, shortness of breath, edema, weakness, blurred vision) and what to do should these symptoms occur, such as calling 911, may help reduce the time it takes to get a patient lifesaving care. Encouraging routine physical health assessments is important to prevent acute, life-threatening events, especially in populations with psychiatric conditions who may not routinely engage with primary care. Identifying interprofessional networks of specialists to assist medically high-risk patients can also help ensure that care is coordinated across all health care providers.

## Case 2 Continued

This 69-year-old patient was diagnosed with an MI and atrial fibrillation and was transferred to a cardiac rehabilitation facility after being stabilized in the hospital. All lab values at discharge are within normal limits. During medication reconciliation preparing the patient for discharge, the patient reports looking forward to using cannabis on the balcony before bed. The patient's current medications include aspirin enteric-coated 81 mg daily, atorvastatin 20 mg daily, warfarin 3 mg daily, lisinopril 40 mg daily, metoprolol succinate 50 mg daily, and paliperidone 6 mg daily.

Drug interactions may result in harm to patients, so these are often an area of emphasis during medication reconciliation appointments. Evaluating the potential for interactions becomes tricky with natural or homeopathic products as there often is limited experience systematically evaluating these products for drug interactions. Cannabis may not be classified as a homeopathic product, but it has similar considerations related to limited information on drug interactions. Additional confounders that may impact a drug interaction evaluation include the variations in the potency of cannabis products and the route of administration, which may influence cannabinoid bioavailability. For cannabis products not obtained from dispensaries, there is the potential for unexpected adulterants, and this may also contribute to safety and interaction concerns. Controlling for all these factors is not realistic, but appreciating the role that cannabis's cannabinoid compounds may play in interacting with concomitant medications is necessary.

Cannabis products may contain more than 500 cannabinoid-type compounds.[54] This paper focuses on the interaction potential of the 2 prominent active compounds, THC and CBD.[54] Pharmacokinetically, medications metabolized by the cytochrome P450 (CYP) enzyme system are targets for interactions by inducers and inhibitors of these enzymes. THC is metabolized hepatically by CYP 2C9, 2C19, and 3A4.[55,56] THC is converted into metabolites including 11-hydroxy-THC, which has been shown to have psychoactive properties.[55-57] Concomitant administration of enzyme inhibitors, such as fluoxetine, may increase THC concentrations, resulting in more adverse effects, whereas inducers such as carbamazepine may result in lower THC concentrations, but because there are active metabolites, the pharmacologic effects may not be altered. CBD is metabolized via CYP 1A1, 1A2, 2C9, 2C19, 2D6, and 3A4 enzymes, making it similarly susceptible to interactions.[55-57] To complicate matters further, multiple cannabinoids, including THC and CBD, are recognized as inhibitors of CYP enzymes. CBD has been identified as an inhibitor of CYP 3A4, and lab evaluations have found that the cannabinoids decreased the activity of CYP 2C19 by 51%, CYP 2C9 and 2D6 by 48%, and CYP 1A2 by 35%.[54,57] There are several case reports of patients controlled on warfarin who used cannabis and subsequently had significant increases in warfarin effects with international normalized ratio (INR) values ranging from 4.6 to 11.55.[58] In another report, a previously controlled patient on warfarin required a dose reduction of 30% after using cannabis to maintain a therapeutic INR.[58] A full evaluation of all drug interactions is beyond the scope of this manuscript, but a list of stronger inducers and inhibitors for cannabis-relevant CYP enzymes are listed in the Table. This is an evolving area; resources such as the Cannabinoid Drug Interaction Review and the Colorado Monitoring Health Concerns Related to Marijuana Drug Interaction Table are valuable websites to supplement tertiary resources when screening for potential interactions with cannabis products.[59,60] For the patient in Case 2, a return to cannabis use will require closer monitoring of the patient's INR due to the potential inhibition of warfarin metabolism by the cannabinoids and subsequent increase in warfarin concentrations. Warfarin is not the only anticoagulant that interacts with cannabis. The activation of clopidogrel or prasugrel may be less effective due to enzyme inhibition.[61] Cannabinoid enzyme inhibition may increase the risk of bleeding for patients on dabigatran, ticagrelor, apixaban, and rivaroxaban, leaving edoxaban the main agent without a noted interaction at this time.[58,61]

Pharmacokinetic interactions are not the only concern in individuals who use cannabis, pharmacodynamic interactions also need to be considered. One such pharmacodynamic interaction with cannabis involves medications that cause sedation. Sedation experienced with cannabis can be more pronounced when it is administered with other central nervous system depressant medications, such as antipsychotics, antihistamines, antiseizure medications, opioids, or alcohol.[57] Cannabinoids have other pharmacologic actions, including agonist actions on the β-adrenergic receptors of the sympathetic nervous system.[61] This agonism along with CB1 receptor activity on cardiac tissue may reduce the efficacy of cardiovascular medications, such as beta-blockers.[57,61]

Collecting a comprehensive medication profile is imperative to identify and resolve potential drug-drug interactions. The

**TABLE: Cannabis drug interactions**[55]

| Enzyme | Substrate | Inducer | Inhibitor | Clinical Intervention With Cannabis Use |
|---|---|---|---|---|
| CYP 1A2 | Apixaban, caffeine, CBD, clopidogrel, clozapine, olanzapine, theophylline | Carbamazepine, omeprazole, phenytoin, rifampin | CBD, THC | Dose reduction may be necessary for substrates of 1A2 with cannabis use. |
| CYP 2C9 | CBD, celecoxib, diclofenac, phenytoin, THC warfarin | Carbamazepine, phenobarbital, phenytoin, rifampin, ritonavir, St. John's wort | CBD, THC | Dose reduction may be necessary for substrates of 2C9 with cannabis use. |
| CYP 2C19 | CBD, clopidogrel, esomeprazole, fluoxetine, THC | Carbamazepine, efavirenz, phenobarbital, phenytoin, rifampin, St. John's wort | CBD, THC | Cannabis may result in decreased efficacy of clopidogrel. Cannabis use with 2C19 substrates may result in increased adverse effects requiring dose reduction. |
| CYP 2D6 | Atomoxetine, CBD, desipramine, dextromethorphan, metoprolol, nebivolol, perphenazine, tolterodine, venlafaxine | Genetic polymorphism | Genetic polymorphism, CBD, THC | Cannabis use with 2D6 substrates may require dose reduction. |
| CYP 3A4 | Atorvastatin, CBD, rivaroxaban, simvastatin, THC | Carbamazepine, phenobarbital, phenytoin, rifampin | CBD | 3A4 inducers may decrease concentrations of CBD or THC, resulting in loss of expected effect. 3A4 inhibitors may increase concentrations of CBD dose reduction may be required. |
| P-glycoprotein | Apixaban, dabigatran, rivaroxaban | | CBD | May result in accumulation of direct oral anticoagulants, which may require dose reduction or switching to an alternative treatment. |

CBD = cannabidiol; THC = tetrahydrocannabinol.

patient in case 2 should be educated on potential interactions with the patient's medications and cannabis. Cannabis may render the metoprolol less effective by competing for beta receptors, resulting in increased heart rate and potential complications from uncontrolled blood pressure or recurrence of arrythmias, but with 2D6 inhibition, metoprolol levels may increase, so monitoring for either increased adverse effects or loss of efficacy will need to be evaluated to determine if dose adjustment or regimen modification is necessary. Atorvastatin metabolism may be inhibited resulting in increased concentrations and potential adverse effects, such as arthralgias or myalgias.[55-58,60] Without intervention, these effects may result in rehospitalization or a subsequent cardiovascular event. Education on interactions allows for discussion of how best to monitor and adjust therapy. For example, metoprolol dose may have to be increased or consider switching to a nondihydropyridine calcium channel blocker following discharge if heart rate and blood pressure become elevated and symptoms of angina or palpitations return. Categorizing patients regularly using cannabis including those with CUD who have chronic health conditions as high risk may help ensure that close monitoring and therapeutic adjustments are being made to medications to promote efficacy and prevent adverse effects.

## Conclusion

The cannabis situation in the United States is continuing to evolve. Cannabis is a Schedule I substance federally, a medicinal agent in at least 40 states with state-specific lists of indications, and a recreational product in at least 24 states and the District of Columbia as of January 2025.[62] The uncertainty regarding its classification and limited knowledge surrounding the effects of cannabis make it difficult for health care providers to effectively monitor and advise patients using cannabis including those with CUD. This provides an opportunity for pharmacists to assist in educating patients, the public, and health care providers on potential risks of cannabis use including drug interactions, mood changes, suicidality and cardiovascular effects.

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