Therapeutic Use of Medical Cannabis in New York State

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Contents

Purpose of This Guideline

This guideline on the therapeutic use of medical cannabis in New York State was developed by the New York State Department of Health AIDS Institute (NYSDOH AI) to accomplish the following:

- Provide clinicians with a framework for implementing the therapeutic use of medical cannabis in their outpatient settings in New York State.

- Increase access to evidence-based medical cannabis treatment for ambulatory patients in New York State by increasing the number of clinicians who can provide that care in outpatient settings (see Increasing Access to Safe Medical Cannabis).

Use of Medical Cannabis in New York State

In 2014, New York State passed the Compassionate Care Act to create a program to safely and effectively provide medical cannabis to eligible state residents. In 2016, the New York State Medical Cannabis Program (NYSMCP) was implemented (see Box 1, below). Through the NYSMCP, the NYSDOH identifies the medical conditions that qualify patients for medical cannabis treatment in New York State (see Box 2: Current Indications for Medical Cannabis Certification in New York State). Trained, registered care providers evaluate patients to determine eligibility for medical cannabis treatment. If eligible, patients are certified and register online to receive a registry identification card that allows them to purchase medical cannabis from a registered dispensary. As of February 2022, more than 124,000 patients have been certified, and more than 3,500 clinicians have registered as medical cannabis providers in New York State. The Public List of Consenting Medical Cannabis Program Practitioners provides registered care providers' names, locations, and contact information.

Registered dispensing facilities in New York State sell medical cannabis products that have been tested by independent third-party laboratories, to ensure the specified delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) content and to detect potential contaminants, and are approved for sale by the Office of Cannabis Management (see Table 2: Medical Cannabis Administration Methods Currently Available in New York State). Available products include oils for vaporization, tinctures, capsules, chewable gels, and whole and ground cannabis flower packaged for use in a vaporizer device. Edible cannabis and cannabis for smoking by combustion are not available by prescription or distributed in registered dispensing facilities. The Marihuana Regulation and Taxation Act (MRTA) introduced home cultivation of medical cannabis for certified patients and caregivers.

In March 2021, legislation legalizing adult cannabis use in New York State was signed, creating the Office of Cannabis Management to implement a comprehensive regulatory framework for medical cannabis use, adult cannabis use, and cannabinoid hemp product use.

Under federal law, per the U.S. Controlled Substance Act, Food and Drug Administration, and U.S. Drug Enforcement Administration, cannabis is "a Schedule I controlled substance with no federally approved medical use for treatment in the U.S."[DEA 2020]. The federal legal status of cannabis has severely limited the ability to conduct high-quality, rigorous research on the medical use of cannabis and limits the availability of published evidence [FDA 2020]. Enforcement of federal cannabis laws is fluid and depends upon Department of Justice enforcement, which changes according to the administration in the Executive Branch [NCSL 2021].

The NYSMCP provides protections to practitioners who abide by program regulations. However, care providers who do not follow NYSMCP program regulations or the MRTA could face legal consequences [New York State Assembly 2014].

Because of the lack of rigorous evidence for the therapeutic use of medical cannabis, some medical organizations recommend against its use, including the American Psychiatric Association, the American Academy of Neurology, and the American Medical Association. However, other professional societies, including the American Society of Addiction Medicine and the American Academy of Family Physicians, have more nuanced policies and recommend that medical cannabis be used only in circumstances in which a true patient—healthcare provider relationship is established with appropriate follow-up and that a health department regulate medical cannabis programs. Ultimately, patients are using and want to use medical cannabis [National Academies of Sciences 2017]. It is important to understand how to discuss it with them and to encourage safe use of medical cannabis as a harm reduction principle or when other treatment modalities have failed.

Box 1: New York State Medical Cannabis Program

The New York State Medical Cannabis Program website offers extensive information and resources to clinicians, including:

- New York State Medical Cannabis Program Laws and Regulations
- Public List of Consenting Medical Cannabis Program Practitioners
- Registered organizations that manufacture and dispense medical cannabis in New York State, and information on product quality, labeling, and safety
- Procedures for clinicians who want to become registered cannabis providers
- For New York State-registered cannabis providers, information on:
  - Patient Certification Instructions
  - Medical Cannabis Adverse Event Reporting Instructions
  - Coverage for Office Visits Related to Medical Cannabis

Medical Cannabis Providers

When indicated, clinicians can refer patients to New York State-registered cannabis providers for assessment and certification. New York State clinicians who wish to become registered medical cannabis providers must complete required training through the NYSMCP; once registered, they can assess patients and recommend cannabis products, delivery methods, initial dosing, and dosing adjustments. Clinicians can either restrict patient certification to certain products or elect to have a pharmacist at the dispensary determine which products a patient can purchase. In New York State, dispensing facilities are required to have a licensed pharmacist on the premises to supervise activity whenever

medical cannabis products are dispensed or handled. These pharmacists have experience with dosing based on individual clinical symptoms and have completed an online curriculum approved by the State.

Definition of Terms

Table 1, below, explains terms used throughout this guideline.

Table 1: Terms Used in This Guideline	
Term	**Definition**
Cannabis and Cannabinoid Products	
Cannabis	A broad term describing various products and chemical compounds derived from the *Cannabis sativa* or *Cannabis indica* species [National Academies of Sciences 2017].
Marijuana	Leaves, stems, seeds, and flower buds derived from the *Cannabis* plant [National Academies of Sciences 2017].
Hemp	*Cannabis* plant with very low levels of THC (<0.3%) [Small 2015].
Unregulated cannabis	Cannabis that is not obtained from a licensed cannabis dispensing facility, does not undergo testing for contaminants or to confirm cannabinoid content by New York State, and is not recommended by a medical care provider.
Regulated adult-use cannabis	Legal cannabis that has undergone testing for contaminants and to confirm cannabinoid content by New York State. Does not require evaluation by a medical care provider to dispense to an individual.
Medical cannabis	Legal cannabis that has undergone testing for contaminants and to confirm cannabinoid content by New York State. Dispensed under the purview of recommendations from a medical care provider.
Dronabinol/nabilone	Orally administered medications with synthetic THC as the active ingredient. Approved by the FDA to treat anorexia associated with weight loss in patients with HIV (dronabinol) and nausea/vomiting associated with cancer chemotherapy in patients who have not responded adequately to conventional antiemetic treatments (dronabinol or nabilone) [FDA 2017; FDA 2006].
Constituents	
Cannabinoid	One of a group of over 100 biologically active chemicals found in the cannabis plant.
delta-9-tetrahydrocannabinol (THC)	The main psychoactive constituent of cannabis [National Academies of Sciences 2017].
Cannabidiol (CBD)	A constituent of cannabis traditionally considered nonpsychoactive [National Academies of Sciences 2017]. A purified form of CBD is approved by the FDA for treatment of seizures associated with Lennox-Gastaut syndrome, Dravet syndrome, or tuberous sclerosis complex in patients 1 year of age and older [FDA(b) 2018].
THC:CBD ratio	The ratio of THC to CBD in a medical cannabis product.
Terpenes	Compounds that produce the plant's smell, taste, and appearance (e.g., limonene, myrcene).
Medical Cannabis Terminology	
Administration method	In New York State, the currently available administration methods for medical cannabis are inhaled, oral, sublingual, topical, and suppository. Inhaled products currently include vaporized oil and vaporized whole or ground flower.
Care provider registration	An educational process by which a medical care provider becomes eligible to certify patients for medical cannabis use.

Table 1: Terms Used in This Guideline	
Term	**Definition**
Medical cannabis certification	A patient assessment completed by a practitioner registered in the New York State Medical Cannabis Program to certify that the patient has a qualifying severe debilitating condition(s) necessary for medical cannabis eligibility in New York State.
Medical cannabis registration	Patients complete the online process to become registered to receive medical cannabis. Once completed, patients receive a New York State registration identification card.
Dispensing facility	A retail site of an organization registered with New York State to dispense medical cannabis under the supervision of a pharmacist to individuals with medical cannabis certification.
Quantification of and Approach to Cannabis Use	
Less frequent or no cannabis use	Cannabis use on *less than 20 days* in a month [Compton, et al. 2016].
Near-daily or heavy cannabis use	Cannabis use on *at least 20 days* of the month [Compton, et al. 2016].
Harm reduction	In the clinical context, an approach and practical strategies targeted to reduce the negative consequences of substance use. It is founded on respect for the rights of individuals who use drugs [adapted from the National Harm Reduction Coalition].
Abbreviation: FDA, U.S. Food and Drug Administration.	

Cannabis Pharmacology and the Endocannabinoid System

"Cannabis" describes a family of plants including *Cannabis sativa, Cannabis indica,* and hemp. The cannabis plant produces more than 100 cannabinoids and a similar number of terpenes. The most widely studied cannabinoids are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD). The other cannabinoids may contribute to the therapeutic effect of cannabis [Huestis 2007], and terpenes (e.g., limonene, myrcene) produce the smell, taste, and appearance of the plant. Cannabinoids can be endogenous (endocannabinoid), plant-derived (phytocannabanoid), or synthetic and act as neurotransmitters within the human endocannabinoid system. Cannabinoid receptors in the endocannabinoid system are called CB1 and CB2 [Munro, et al. 1993] [Matsuda, et al. 1990].

CB1 receptors exist primarily in areas of the brain that regulate appetite, memory, fear, and motor responses. Stimulation of CB1 receptors in the brain produces psychotropic effects. CB1 receptors are also found outside the brain in the gastrointestinal tract, adipocytes, liver, and skeletal muscle [Mackie 2005; Matsuda, et al. 1990]. CB2 is primarily expressed in macrophages and other macrophage-derived cells that are part of the immune system [Munro, et al. 1993].

Current understanding of cannabis pharmacology is incomplete, and much remains under investigation. Both THC and CBD act on CB1 and CB2 receptors but in different ways. THC is a partial agonist of CB1 and CB2 receptors. Stimulation of these receptors by THC leads to analgesic, anti-inflammatory, and muscle-relaxant effects [Pertwee 2006]. The binding of THC to CB1 receptors is associated with psychoactive features, including reduced or enhanced anxiety, memory suppression, euphoria, and intoxication. Stimulation of CB2 receptors leads to anti-inflammatory effects [Russo and Guy 2006]. CBD binds weakly to CB1 and CB2 receptors [Russo and Guy 2006], producing anti-inflammatory [Ben-Shabat, et al. 2006], antispasmodic [Wade, et al. 2006], and analgesic effects [Maione, et al. 2011]. When THC and CBD are used together, several other receptors are activated to regulate pain perception [Russo and Guy 2006].

Therapeutic Uses of Cannabis

Evidence supporting the most common current uses of medical cannabis is summarized below. To be certified for medical cannabis use in New York State, patients must have a qualifying condition, which are detailed in Box 2, below, and based on New York State legislation. The Marihuana Regulation and Taxation Act (MRTA), signed into law March 31, 2021, expands the medical program to include Alzheimer disease, muscular dystrophy, dystonia, rheumatoid arthritis, and autism as qualifying conditions. The MRTA also affords providers the authority to use their clinical discretion to certify

their patients for any other condition for which the patient is likely to receive therapeutic or palliative benefit from the primary or adjunctive treatment with medical cannabis. Consult the New York State Medical Cannabis Program website to find the most up-to-date list of qualifying conditions.

Box 2: Current Indications for Medical Cannabis Certification in New York State (as of January 2022) See New York State Medical Cannabis Program for the most up-to-date information.
Qualifying Conditions (*Must be specified in the patient health care record.*)
Chronic pain
Pain that degrades health and functional capability as an alternative to opioid use
Post-traumatic stress disorder
Substance use disorder
Neuropathies
Epilepsy
Cancer
HIV infection or AIDS
Amyotrophic lateral sclerosis
Parkinson disease
Multiple sclerosis
Spinal cord injury with spasticity
Inflammatory bowel disease
Huntington disease
Alzheimer muscular dystrophy
Dystonia
Rheumatoid arthritis
Autism
Any other condition at the discretion of the care provider

Previously, the program had a list of associated conditions that were required for patient certification in addition to the qualifying conditions (including opioid use disorder, post-traumatic stress disorder, seizures, severe nausea, severe or persistent muscle spasms, severe or chronic pain resulting in substantial limitation of function, and cachexia or wasting syndrome). Associated conditions are no longer required under the MRTA.

Chronic or severe pain: The most common condition for which patients are certified to receive medical cannabis in New York State is chronic or severe pain [NYSDOH 2018] that degrades health and functional capability and might otherwise be treated with opioids. A systematic review of randomized controlled trials (RCTs) found that, compared with placebo, the use of cannabinoids is more likely to result in ≥30% reduction in pain scores [Whiting, et al. 2015]. Of the 28 RCTs reviewed, 22 evaluated plant-derived cannabinoids and most used a placebo control. Most studies used a plant-derived medical cannabis product developed for medical use outside of the United States. The remainder evaluated cannabis in flower form, which can be obtained for research studies from the National Institute on Drug Abuse [National Academies of Sciences 2017].

Severe or persistent muscle spasms: Cannabinoid use for the management of spasticity has been studied primarily in people with multiple sclerosis (MS). One systematic review identified 27 studies (8 RCTs) examining spasticity in adults [Nielsen, et al. 2019]; 21 of these studies included adults with MS. Spasticity improved in participants in the 8 RCTs, although spasticity improvement was based on participant- rather than clinician-rated measures, and the few RCTs that used clinician-rated measures for spasticity used the now outdated Modified Ashworth Scale [Nielsen, et al. 2019; Ansari, et al. 2006]. In another meta-analysis, investigators conducted a pooled analysis of data from 3 studies that used numerical rating scales in investigating the efficacy of cannabinoids for spasticity in MS [Whiting, et al. 2015]. Compared

with placebo, formulations of cannabis with delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) were associated with improved spasticity on a participant-reported rating scale, and greater improvements in symptoms were reported by participants who received coformulated THC and CBD (compared with those who received THC alone).

As with the research on chronic pain, these studies were all conducted with forms of medical cannabis that are not the same as those provided to medical cannabis patients in New York State. However, the cannabis studied contained the same primary active ingredients (THC and CBD) as the medical cannabis currently available in New York State.

Post-traumatic stress disorder (PTSD): PTSD was added as a qualifying condition for the New York State Medical Cannabis Program (NYSMCP) in November 2017. The efficacy of cannabis for managing PTSD is not well studied [Lowe, et al. 2019]. Several small studies have examined THC for the treatment of nightmares, insomnia, and other PTSD symptoms, mostly in combat veterans [Jetly, et al. 2015; Cameron, et al. 2014; Roitman, et al. 2014; Fraser 2009]. In all of these studies, participants experienced improved sleep, as measured by a reduction in the number or intensity of nightmares or improvements in overall sleep quality. Concern remains that cannabis use in people with PTSD may result in adverse outcomes; however, this is also not well studied [Lowe, et al. 2019].

Severe nausea: Few studies have examined medical cannabis use to treat severe nausea [National Academies of Sciences 2017]. Oral synthetic THC (nabilone or dronabinol) has been used to treat chemotherapy-induced nausea for decades. It is superior to placebo and equally efficacious to comparator antiemetics [Grotenhermen and Müller-Vahl 2012]. CBD is less well studied in humans for the management of nausea than THC. In animal studies, CBD alone was an effective anti-nausea agent [Whiting, et al. 2015; Rock, et al. 2012].

Cachexia or wasting: There is very limited evidence that cannabis is effective in the management of cachexia or wasting. The use of cannabis for cachexia or wasting has been studied primarily in either AIDS wasting syndrome or cancer-associated cachexia. In an article summarizing 4 RCTs that investigated the effect of cannabis in individuals with AIDS wasting syndrome, the author concluded that these trials had a high risk of bias, but there is some evidence that cannabis is effective for weight gain in individuals with HIV [Whiting, et al. 2015]. All 4 of these studies compared dronabinol (synthetic THC) with placebo or megestrol acetate. For cancer-associated cachexia, a phase 3 multicenter RCT compared treatment with cannabis extract (THC and CBD), THC alone, and placebo for 6 weeks. Participants (164 total) were monitored for appetite, mood, and nausea, with no significant differences between the 3 groups. Recruitment was terminated early because the data review board determined differences between groups were unlikely to emerge [Strasser, et al. 2006]. In a more recent pilot study, 17 individuals with cancer-associated cachexia were enrolled and received high THC:low CBD cannabis capsules for 6 months. Only 6 participants completed the study, 3 of whom had a weight gain of ≥10% from baseline; weight remained stable in the other participants [Bar-Sela, et al. 2019].

Seizures: In June 2018, CBD was approved by the U.S. Food and Drug Administration to treat rare forms of childhood epilepsy: Dravet syndrome, Lennox-Gastaut syndrome, and tuberous sclerosis complex [FDA(a) 2018]. Dravet syndrome is a complex childhood epilepsy disorder associated with treatment-resistant seizures and a high mortality rate. In a double-blind RCT, daily oral CBD was associated with a statistically significant reduction in the frequency of convulsive seizures [Devinsky, et al. 2017]. In Lennox-Gastaut syndrome, another childhood epilepsy disorder with treatment-resistant seizures, CBD use resulted in a 41% reduction in seizure frequency. Reduction in seizure frequency was dose-dependent [Devinsky, et al. 2018].

The use of cannabinoids to manage seizures in adults and children with more common forms of epilepsy is not as well studied. In an open-label study of CBD use in 70 pediatric and 62 adult participants with treatment-resistant epilepsy, 64% of participants experienced at least a 50% reduction in seizure frequency. Participants also experienced reduced severity of seizures and fewer adverse events [Szaflarski, et al. 2018]. In a small study of 21 adult participants with treatment-resistant seizures, CBD use was associated with a 71% reduction in seizure frequency, an 80% reduction in seizure severity, and improved mood [Allendorfer, et al. 2019]. These outcomes are very encouraging but were achieved with doses of CBD alone that exceed the doses approved for sale by the NYSMCP. Beyond CBD, there is little evidence to support taking other cannabinoids to manage seizures [Perucca 2017].

Opioid use: Medical cannabis treatment has emerged as a strategy to address the opioid epidemic. Amendments to the New York State Medical Use of Marijuana regulations in 2018 added substance use disorder as a serious condition that qualifies for medical cannabis use (see Box 2, above) [NYSDOH 2018].

In several ecological studies, medical cannabis use has been associated with reduced opioid-related deaths, opioid prescribing, and opioid use [Bradford, et al. 2018; Powell, et al. 2018; Bradford and Bradford 2017; Boehnke, et al. 2016; Bachhuber, et al. 2014]. However, more recent studies found that opioid overdose mortality increased in U.S. states where medical cannabis is available [Shover, et al. 2019; Caputi and Humphreys 2018]. Because these studies were retrospective and observational, it is impossible to eliminate confounding factors and determine causality. The observed benefits of cannabis on opioid-related pain outcomes are due to its analgesic effect, but evidence to support taking medical cannabis to treat opioid use disorder (OUD) is scant. Randomized controlled clinical trials are needed to understand the relationship between medical cannabis use and opioid-related outcomes.

There are well-established OUD treatments based on a strong evidence base. Buprenorphine and methadone are the standard of care for OUD and are effective in retaining patients in treatment and reducing illicit opioid use [Mancher and

Leshner 2019; Hser, et al. 2016; Timko, et al. 2016; Mattick, et al. 2014; Fiellin, et al. 2011; Kakko, et al. 2003]. If there is a role for medical cannabis in OUD management, it will be to augment rather than replace evidence-based pharmacologic treatment. Currently, there is insufficient evidence to advocate for the use of medical cannabis to manage OUD.

Medical Cannabis Formulations and Administration Methods Available in New York State

All medical cannabis products sold in dispensing facilities in New York State must meet specific manufacturing requirements regulated by the New York State Office of Cannabis Management. These requirements address methods for extracting cannabinoids from cannabis plants, the cannabinoid profile, the presence of additives, and labeling. All cannabis manufacturers must provide medical cannabis products that are equal parts delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) and low THC:high CBD (e.g., a 1:20 ratio of THC to CBD). All medical cannabis dispensing facilities also sell high THC and low CBD products, currently the most frequently used products by individuals in New York State. All products are tested by a laboratory located in New York State and licensed by the Bureau of Narcotic Enforcement to confirm cannabinoid content and identify contaminants [NYSDOH 2020].

Medical cannabis administration methods available to individuals in New York State are summarized in Table 2, below. As of September 2021, the Commissioner of Health had approved metered liquid or oil preparations, solid and semi-solid preparations (capsules, chewable and effervescent tablets, lozenges), metered ground plant preparations, topical forms, and transdermal patches. In early October 2021, whole flower cannabis for vaporization was added as an approved form. The potential harms vary by administration method. Smoking ground flower through combustion—which is not currently legal in New York State—confers the highest risk of harm because of the high temperature of inhaled smoke and potential for chronic damage to bronchioles and airways [Ribeiro and Ind 2018]. Risk is lower when cannabis is vaporized rather than smoked via combustion. Table 2, below, outlines the advantages and disadvantages of each administration method.

Hemp-based CBD versus medical cannabis: The 2018 U.S. Farm Bill Act made it legal to develop, distribute, sell, and market CBD products derived from hemp plants, which contain less than 0.3% THC. The Farm Bill Act removed hemp-based CBD regulation from the purview of the U.S. Food and Drug Administration and Schedule I status (Schedule I drugs, substances, or chemicals are defined as drugs with no medical purpose and a high potential for abuse). Hemp-based CBD has subsequently become available for purchase in retail settings, such as grocery and convenience stores, and with many different product types, including foods and beverages. Unregulated hemp-based CBD is often inaccurately labeled [Vandrey, et al. 2008]. One study found that almost half of products contained less CBD than the label described, and an additional quarter contained more CBD. In one-fifth of products sampled, THC was detected [Bonn-Miller, et al. 2017].

Table 2: Medical Cannabis Administration Methods Currently Available in New York State (as of January 2022)			
Product, Method of Use, and Bioavailability	**Bioavailability and Peak or Onset and Duration of Effect**	**Advantages**	**Disadvantages** (also see guideline section Medical Cannabis Initiation)
Vaped oil: Inhaled using a battery-operated, portable pen-like device that administers a metered dose	• **Bioavailability:** Varies between 2% to 56% due to difference in inhalation dynamics (number of puffs, spacing of puffs, hold time, inhalation time, etc.) [a] • **Peak:** 9 minutes [a] • **Duration:** ≤2 hours [a]	• Quick onset of action • Ease of dose titration	Potential for short- and long-term adverse effects: • Intoxication [b] • Chronic bronchitis [c]
Vaped ground or whole flower: Inhaled using a tabletop or handheld device that creates vapor from the plant material and provides metered doses	• **Bioavailability:** Varies between 2% to 56% due to difference in inhalation dynamics (number of puffs, spacing of puffs, hold time, inhalation time, etc.) [a] • **Peak:** 9 minutes [a] • **Duration:** ≤2 hours [a]	• Quick onset of action • Ease of dose titration • No oil or additives in the flower	Potential for short- and long-term adverse effects: • Intoxication [b] • Chronic bronchitis [c]

Table 2: Medical Cannabis Administration Methods Currently Available in New York State (as of January 2022)			
Product, Method of Use, and Bioavailability	**Bioavailability and Peak or Onset and Duration of Effect**	**Advantages**	**Disadvantages** (also see guideline section Medical Cannabis Initiation)
Capsule/tablets/chewable tablets/orally disintegrating tablets/effervescent tablets/dissolvable powder/chewable gels: Oral ingestion	• **Bioavailability:** 4% to 25% depending on the study [d]. Variable due to drug degradation in the stomach, variable absorption in the stomach, and first-pass metabolism • **Peak:** 1-5 hours [e] • **Duration:** ≤25 hours [e]	• Slow onset of action, low bioavailability • Avoids adverse effects of inhalation • Long duration of effect could be advantageous in certain clinical situations	• Risk of dose stacking—repeating doses before an effect is felt. Usually attributable to a long period before onset of effect. Results in unanticipated intoxication and adverse effects [b,d] • Absorption and onset and duration of effect can vary based on individual patient factors (e.g., fat content of meals, patient weight) • Difficult to titrate
Tincture and spray: Sublingual/oral	• **Bioavailability:** 87.5% to 90% [f] • **Onset:** As early as 10 min [f,g] • **Duration:** ≤10 hours [f]	• Fast onset of action • Avoids adverse effects of inhalation • Advantageous for patients with swallowing difficulties	• Taste • Potential for user error because patients can swallow the product rather than wait for absorption through oral membranes
Suppository: Rectal	• **Bioavailability:** 14% to 67% [h,i] • **Onset:** 1-2 hours [j] • **Duration:** ≤8 hours [j]	• Avoids first-pass metabolism [j] • Avoids adverse effects of inhalation	• Inconvenient dosing method • Very little supporting data for the use of suppositories
Lotions, gels: Transdermal	• **Bioavailability:** Depends on formulation. Data is extrapolated from animal models. There may be wide variability in effect onset based on formulation, heat application, and amount of fat in tissue where applied [k] • **Onset:** 2 hours [l] • **Duration:** ≤48 hours [l]	• Avoids adverse effects of inhalation • Helpful for patients unable to adhere to other formulations (terminal illness, etc.)	Variability of bioavailability depending on formulation [l]

References:

a. [Huestis, et al. 1992]
b. [Monte, et al. 2019]
c. [Mancher and Leshner 2019]
d. [Monte, et al. 2015]
e. [Goodwin, et al. 2006; Gustafson, et al. 2003; Wall, et al. 1983; Ohlsson, et al. 1980; Perez-Reyes, et al. 1973]

f. [Hilliard, et al. 2012; Karschner, et al. 2011]
g. [Guy and Robson 2004]
h. [ElSohly(a), et al. 1991]
i. [ElSohly(b), et al. 1991]
j. [Mattes, et al. 1993]
k. [Huestis 2007]
l. [Valiveti, et al. 2004]

Assessment

☑ RECOMMENDATIONS

Assessment

- Before approving a patient for medical cannabis use, clinicians should determine the following:
  - Current and previous use of medical, unregulated, and regulated adult-use cannabis, including amount and administration method (A3)
  - Method used for smoking cannabis (e.g., pipe or rolling papers), if applicable (A3)
  - Known history of arrhythmia, CAD, or psychosis (A2)
  - Potential drug-drug interactions with medical cannabis (A*)
- Clinicians should assess and document the qualifying condition for medical cannabis based on medical records and patient evaluation with standardized tools (A*), such as:
  - PEG Scale
  - DSM-5 PTSD Checklist

Abbreviations: CAD, coronary artery disease; DSM, Diagnostic and Statistical Manual of Mental Disorders; PEG, Pain, Enjoyment of Life, and General Activity.

Box 3: Good Practice for Medical Cannabis Assessment

- Obtain the following information from patient interviews, medical records, and, when possible, the patient's care providers (e.g., primary care, psychiatry, neurology, pain management, oncology, infectious disease):
  - A thorough history of the condition for which the patient seeks medical cannabis. Onset, duration, and characteristics should be described as well as previous treatment attempts and their success.
  - Psychiatric history, including diagnoses, history of psychosis, previous treatment(s), hospitalization(s), signs and symptoms (e.g., auditory or visual hallucinations), history of suicide attempts or suicidal ideation, and family history of schizophrenia or other psychosis.
  - A detailed history of current and prior substance use, SUD, and treatment. Family history of SUD should be documented. Tools for diagnosing SUD include the CUDIT-R and the DSM-5; however, these tools are not standardized for use with medical cannabis [Sagar 2021].
  - Prior medical history and full medication reconciliation. This should include checking the New York State I-STOP/PMP - Internet System for Tracking Over-Prescribing - Prescription Monitoring Program to identify other controlled substances the patient takes, including medical cannabis.
- Check whether patients have a state photo ID and email address and that their current address matches their state ID. If they do not have a state photo ID, they must submit a different proof of New York State residence. Patients must complete online registration after receiving their certification. Registration may be completed by telephone if a patient does not have internet access, but the required documents must be mailed for processing, along with an attestation form provided with the certification.

Abbreviations: CUDIT-R, Cannabis Use Disorder Identification Test-Revised; DSM, Diagnostic and Statistical Manual of Mental Disorders; SUD, substance use disorder.

Current amount and method of cannabis use: If patients are currently using medical, regulated adult-use, or unregulated cannabis, care providers should ask patients to describe their use in detail, including the amount and frequency of cannabis used daily, estimated delta-9-tetrahydrocannabinol (THC) level, other cannabinoids (e.g., delta-8-tetrahydrocannabinol) in consumed cannabis (if known), and the type and method of use. Details about a patient's current pattern of cannabis use inform the recommended dose and type of medical cannabis and the recommended method for use.

If patients smoke cannabis, clinicians should ask about the method used, such as rolling papers, water pipe (bong), pipe, or vaporizer. Other methods include using cigar papers to roll a large "blunt" and smoking a combination of cannabis and

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tobacco, which may result in nicotine dependence and require nicotine replacement therapy if switching to a form of cannabis that does not include nicotine.

Regulated cannabis versus unregulated cannabis: Medical and regulated adult-use cannabis may be less harmful than unregulated cannabis because they have known THC and cannabidiol (CBD) content, are tested for potential contaminants, and can be purchased legally [NYSDOH 2020]. Regulated THC and CBD levels and ratios and doses in milligrams allow patients to titrate the dose of cannabis more precisely than is possible with unregulated cannabis. If a patient uses unregulated cannabis before initiating medical cannabis for a qualifying condition, a primary harm reduction goal may be to switch to medical cannabis. Clinicians can work with patients on limiting THC content and potentially harmful psychoactive effects while addressing symptoms of the presenting condition.

By acquiring medical cannabis at registered dispensing facilities, individuals can limit interactions with the street market and the criminal justice system. The criminalization of cannabis has a disproportionately negative effect on Black and Hispanic people; in New York State, in 2018, the arrest rate for cannabis possession was 2.6 times higher among Black people than White people, with rates ranging widely among counties [ACLU 2020].

Conditions that require caution: Clinicians should determine if the patient seeking medical cannabis has a history of arrhythmia, CAD, or psychosis. Based primarily on limited evidence on the effects of THC, caution should be used when recommending medical cannabis treatment to patients with these conditions [Athanassiou, et al. 2021; Skipina, et al. 2021; Yahud, et al. 2020; Goyal, et al. 2017; Shrivastava, et al. 2014]. Acute THC exposure has been associated with tachycardia and developing or worsening psychosis [Bryson and Frost 2011; Khiabani, et al. 2008; Sewell, et al. 2008]. If arrhythmia, CAD, or psychosis is identified during evaluation for medical cannabis use and the patient is not being treated for the condition, refer the patient for treatment as appropriate. If the patient is already receiving treatment for the condition, consult with the treating clinician.

The following patient characteristics or conditions may affect the safety of medical cannabis treatment and should be carefully evaluated: personal history of substance use disorder (SUD), family history of schizophrenia [Shrivastava, et al. 2014], personal history of hallucinations [Shrivastava, et al. 2014], and risk factors for cardiac disease [Goyal, et al. 2017]. Safety concerns associated with these factors are based on limited evidence that acute THC exposure is associated with tachycardia and developing or worsening psychosis [Bryson and Frost 2011; Khiabani, et al. 2008; Sewell, et al. 2008]. History of SUD is considered a relative contraindication to medical cannabis because of concerns that individuals who use medical cannabis may be at increased risk for cannabis use disorder. However, in patients who are already using unregulated cannabis, medical cannabis certification could support harm reduction.

Cannabis use during pregnancy also warrants careful evaluation [English, et al. 1997]. Chronic THC exposure during pregnancy has been associated with preterm labor and intrauterine growth retardation [Gunn, et al. 2016]. For additional discussion of pregnancy, see the guideline section Medical Cannabis Initiation.

Potential drug-drug interactions: There is a paucity of evidence on potential drug-drug interactions with medical cannabis. THC and CBD are metabolized in the cytochrome P450 (CYP450) system and may inhibit the metabolism of other strong CYP450 inhibitors, such as warfarin [Damkier, et al. 2019; Alsherbiny and Li 2018]. Cannabis can also have additive sedative effects when used with other sedating agents [Echeverria-Villalobos, et al. 2019; Russo 2016]. Cannabis and alcohol used in combination are associated with increased impairment of complex task performance, such as driving, compared with cannabis or alcohol use alone [Miller, et al. 2020]. To check for potential drug-drug interactions with medical cannabis, see Colorado Department of Public Health and Environment Monitoring Health Concerns Related to Marijuana: Drug Interaction Table.

Assess for qualifying conditions with standardized tools. Clinicians should assess the condition for which patients seek medical cannabis and other conditions that may be affected by cannabis treatment with standardized instruments at baseline and follow-up visits. Changes in test scores can indicate response to medical cannabis treatment and whether it is advisable to change dosage or formulation. Standardized tools include the PEG Scale [Krebs, et al. 2009] and the DSM-5 PTSD Checklist [Lang, et al. 2005].

Cost of medical cannabis: The typical cost of a 30-day supply of a starting dose of medical cannabis from a dispensary ranges from $70 to $150. Medical cannabis is not covered by insurance and must be paid for with cash or a debit card, which may pose significant barriers to access. Care providers should ensure that patients seeking medical cannabis certification are informed about cost and payment requirements.

Medical Cannabis Initiation

☑ RECOMMENDATIONS

Medical Cannabis Initiation

- Clinicians should recommend a medical cannabis formulation and dose based on a patient's symptoms and the frequency, amount, and type of cannabis currently in use, if applicable. (A3)
- Clinicians should use caution when recommending medical cannabis to patients with a known history of arrhythmia or CAD, a history of psychosis, or a family history of schizophrenia (A2):
  - For a patient with a history of arrhythmia or CAD, the clinician should determine whether the patient is being treated for the condition and consult the treating care provider. In discussing the risks and benefits of medical cannabis use, clinicians should inform patients that the THC in medical cannabis can elevate heart rate.
  - If a patient has a history of psychosis and is being treated for the condition, the clinician should consult the patient's mental health care provider to determine the context of the psychosis (e.g., substance-induced) and inform the patient that the THC in medical cannabis can exacerbate psychosis.
  - If a patient has active psychosis and is cannabis-naive, the clinician should advise against initiating medical cannabis; if a patient is using unregulated cannabis, the clinician should recommend switching to medical cannabis to reduce THC intake and discuss harm reduction strategies with the patient.
  - If a patient has a family history of schizophrenia, the clinician should inform the patient that cannabis use may precipitate symptoms of schizophrenia.
- Clinicians should counsel patients on the risks and benefits of the available medical cannabis administration methods (see Table 2: Medical Cannabis Administration Methods Currently Available in New York State). (A*)
- Clinicians should advise patients against using vaped or smoked cannabis products. (A*)
- Clinicians should inform patients about potential acute adverse effects of medical cannabis use and provide patient education regarding management of adverse effects (A2):
  - Clinicians should inform patients of the potential for intoxication (i.e., feeling "high"), dizziness, or impairment in concentration; if symptoms occur, recommend that patients lie down and wait for symptoms to resolve and reduce their dose of THC.
  - Clinicians should ensure that patients know to seek emergency medical evaluation if they experience any serious adverse effects, including hallucinations, psychosis, severe anxiety, paranoia, pulmonary or cardiac symptoms, or hyperemesis.
  - Clinicians should inform patients that cannabis use may increase the risk of falls, particularly in elderly individuals.
- Clinicians should inform patients of childbearing potential of the potential risks of using cannabis while pregnant, including preterm labor and intrauterine growth restriction (A2):
  - If a cannabis-naive patient is pregnant, the clinician should advise against initiating any cannabis use.
  - If a pregnant patient is currently using unregulated cannabis, the clinician should first advise against continued use. If the patient plans to continue using cannabis, the clinician should encourage a switch to regulated adult-use or medical cannabis and discuss harm reduction strategies.
  - For individuals who could become pregnant, clinicians should recommend the use of contraception while using cannabis.
- Clinicians should inform patients who are <25 years old of the potential for long-term changes in brain development, mental health, and cognition associated with cannabis use in people whose brains are still developing (see guideline section Monitoring > Cognition) (A2):
  - If a cannabis-naive patient is <25 years old, the clinician should advise against initiating cannabis.
  - If a patient <25 years old is currently using unregulated cannabis and intends to continue use, the clinician should advise the patient to switch to regulated adult-use or medical cannabis and discuss harm reduction strategies.
- Clinicians should advise patients to take the first dose of medical cannabis before bedtime and at home in a safe environment to limit potential immediate adverse effects. (A3)

☑ **RECOMMENDATIONS**

- Clinicians should caution patients about the potential for impaired driving while taking cannabis and advise them to avoid driving or operating heavy machinery while using medical cannabis. (A2)
- Clinicians should inform patients of the risks associated with unregulated cannabis and recommend discontinuation after medical cannabis is initiated. (A3)

Abbreviations: CAD, coronary artery disease; THC, delta-9-tetrahydrocannabinol.

Clinicians do not *prescribe* a specific formulation and dosage of cannabis; they *recommend* it. Clinicians can manage all aspects of medical cannabis treatment or limit their practice to assessment and certification and refer patients to dispensary pharmacists for all other related services (formulation, initial dosing, and dosing adjustments based on individual symptoms). Because clinicians have knowledge of or access to a patient's medical history, comorbidities, and history of cannabis use, it is preferable for clinicians to direct formulation, initial dosing, and dosing adjustments for patients' medical cannabis use and collaborate with the medical cannabis dispensary pharmacist as needed. If clinicians make specific recommendations in their certification, dispensary pharmacists are bound by law to follow those instructions (see New York State Medical Cannabis Program Patient Certification Instructions).

After clinician certification, patients must complete an online registration to link the certification to their state ID. If they do not have a state ID, they must send proof of residence to the NYSDOH. This is usually done electronically via the Medical Cannabis Data Management System. Patients with poor technological literacy may need assistance with this process.

Because of a lack of high-quality evidence, specific dosing regimens for the therapeutic use of medical cannabis are lacking. The authors have been managing patients with medical cannabis since 2016 when the Montefiore Medical Center Medical Cannabis Program was implemented. Boxes 4 and 5, below, outline basic strategies for implementing medical cannabis treatment based on the authors' clinical experiences.

Box 4: Good Practice for Implementation of Medical Cannabis Treatment [a]

- Consider recommending medical cannabis to patients who meet the legal criteria (see Box 2: Current Indications for Medical Cannabis Certification in New York State) and have ongoing symptoms that have not been successfully managed with other treatments.
- Recommend a cannabis formulation (THC:CBD) based on a patient's level of use at assessment:
    - Less frequent to no use (<20 days/month): 1 THC:1 CBD
    - Near-daily to heavy use (≥20 days/month): High THC:low CBD
    - Some patients with severe pain may require high THC:low CBD regardless of current use.
- Recommend induction with the lowest dose possible for the first 2 to 3 days of use. The daily dose may be increased by 2.5 mg to 5 mg every 2 to 3 days, as needed, until a therapeutic level is reached.
    - Advise patients that incremental dosing can help prevent cannabis-related adverse events.
    - Encourage patients to maintain close contact with dispensary pharmacists or their medical care providers during the induction period.
    - Advise patients that total dose and dosing frequency can be increased if needed.
- For cannabis-naive patients, recommend an initial dose of 2.5 mg total cannabinoids daily.
- For cannabis-experienced patients, recommend an initial dose of 5 mg to 10 mg total cannabinoids daily.
- For patients who are currently using cannabis, calculate the dose based on the following:
    - Estimate the amount of total cannabinoids and THC used daily (see Box 5, below).
    - Recommend a dose of medical cannabis equivalent to at least 50% of the patient's current amount of THC to reduce the risk of THC withdrawal symptoms.

Abbreviations: CBD, cannabidiol; THC, delta-9-tetrahydrocannabinol.
Note:
a. Based on experience at Montefiore Medical Center Medical Cannabis Program.

Box 5: Sample Approach to Quantifying Current Cannabis Use and Determining Medical Cannabis Dose [a]

- Total cannabinoids combine THC and CBD:
  - 1 vape inhalation of cannabis = 10 mg total cannabinoids
  - 1/8 ounce of cannabis = 3,500 mg total cannabinoids
  - 1 ounce of cannabis = 28,000 mg total cannabinoids
- Assumption: Most unregulated cannabis is 10% THC [b]. This may be an underestimation of current street cannabis composition; however, it is used to approximate a patient's THC dose so an appropriate medical regimen can be recommended.
- *Example 1:* A patient who reports using 1/8 ounce of cannabis monthly uses approximately 3,500 mg total cannabinoids (or 350 mg THC) monthly.
  - This amount is equivalent to approximately 117 mg total cannabinoids daily or approximately 12 mg of THC daily.
  - An appropriate recommendation for this patient would be a volume of tincture containing 10 mg of THC daily, taken either in 1 dose at night or in divided doses 2 to 3 times daily.
- *Example 2:* A patient who reports using 1 ounce of cannabis monthly uses approximately 28,000 mg total cannabinoids (or 2,800 mg THC) monthly [b].
  - This amount is equivalent to approximately 930 mg of total cannabinoids daily or 93 mg of THC daily.
  - An appropriate recommendation for this patient would be 40 mg to 50 mg of THC daily, taken in 10 mg doses every 4 to 6 hours.
  - Counsel patient to reduce nonmedical cannabis use.

Abbreviations: CBD, cannabidiol; THC, delta-9-tetrahydrocannabinol.

Notes:
a. The calculations and doses presented are based on experience at Montefiore Medical Center Medical Cannabis Program.
b. To calculate an initial dose, it is estimated that street cannabis in New York State is approximately 10% THC [ElSohly, et al. 2016]. The percentage may change over time and by geographic region.

Initial dosage: For cannabis-naive patients, the lowest possible dose of 2.5 mg THC daily is recommended. For cannabis-experienced patients, clinicians should recommend an initial dose of 5 mg to 10 mg of total cannabinoids daily. For patients currently using cannabis, the overall goal is to reduce THC use and limit intoxication. After estimating the current daily dose of total cannabinoids and THC (see Box 4, above), clinicians should recommend an initial dose equivalent to at least 50% of the patient's current daily amount of THC to minimize withdrawal symptoms, which may include irritability, sleeplessness, and decreased appetite [Vandrey, et al. 2008].

Induction: Clinicians should advise patients to initiate medical cannabis at the lowest possible dose and slowly titrate up. Patients should take their initial dose at night and maintain that dose for 2 to 3 days. After that period, the dose can be increased by 2 mg to 5 mg THC daily. Patients can continue to increase the dose every 2 to 3 days until a therapeutic level is reached. If symptoms are experienced during the day, a midday or morning dose can be added. Clinicians should advise patients to maintain direct contact with pharmacists at the dispensary or with their certifying medical cannabis providers during the induction period to report any adverse events and address any dosing concerns.

Conditions that require caution in dosing and induction: Clinicians should use caution when recommending medical cannabis to patients with a known history of arrhythmia, CAD, or psychosis (see guideline section Assessment > Conditions that require caution). As with all patients initiating medical cannabis, clinicians should advise patients with these conditions to start at a low dose and increase their dose cautiously every 2 to 3 days.

Pregnancy: In patients who are pregnant or of childbearing potential, clinicians should discuss the risks of preterm labor and intrauterine growth restriction associated with cannabis use and advise against use of cannabis during pregnancy [Gunn, et al. 2016]. There is no evidence to support use of medical cannabis to manage pregnancy-associated nausea and vomiting. In patients who are pregnant and who are not already using cannabis, clinicians should advise against initiating medical cannabis. In patients who are pregnant and using unregulated cannabis, clinicians and patients may find a harm reduction perspective useful. Patients may be using unregulated cannabis to treat specific symptoms such as PTSD, and medical cannabis may be the safer choice if a patient plans to continue using cannabis. For individuals who could become pregnant, clinicians should recommend the use of contraception while using medical cannabis.

Adverse effects: Clinicians should advise patients initiating medical cannabis to take the first dose at night to limit potential adverse effects, such as feeling high, dizzy, or unable to concentrate.

Severe adverse effects usually present as anxiety, paranoia, or panic attacks. Other neurologic symptoms include euphoria, lightheadedness, dizziness, or vertigo. In most cases, these symptoms require no intervention and are managed through observation. Rarely, cannabis can cause immediate nausea, vomiting, or abdominal pain, which can be managed with symptomatic treatment such as antiemetics [Noble, et al. 2019]. To date, there are no known cases of fatal overdose from cannabis use [Hasin 2018], but heavy cannabis use has been linked to increased healthcare utilization in states with legalized cannabis use, particularly among those using cannabis through oral rather than inhaled routes [Monte, et al. 2019].

There is concern that cannabis intoxication will lead to motor vehicle accidents [Brady and Li 2014]. Cannabis use impairs driving in a dose-response manner [Hartman and Huestis 2013]. However, population-level studies have shown a mixed relationship between medical cannabis laws and increased motor vehicle accidents or traffic fatalities [Rogeberg 2019; Santaella-Tenorio, et al. 2017; Dubois, et al. 2015; Pollini, et al. 2015; Masten and Guenzburger 2014; Blows, et al. 2005]. Clinicians should caution patients about the potential for impaired driving while using cannabis and advise patients to avoid driving or operating heavy machinery if physical or mental control is diminished by cannabis use. Clinicians should emphasize that combining cannabis with alcohol can impair complex task performance, such as driving [Miller, et al. 2020]. It is also important to advise patients to store cannabis in a location that is safe from children and pets.

Follow-up: Individualized, ongoing follow-up is essential for support and modification of the treatment plan as indicated. Follow-up within 2 weeks of treatment initiation provides the opportunity to adjust a patient's treatment plan based on initial experience. As treatment continues, the frequency of follow-up can be tailored to a patient's specific needs and in accordance with the clinic's existing policies regarding treatment and follow-up for patients taking other controlled substances. In the absence of an existing policy, this committee suggests clinical follow-up every 3 to 6 months.

Monitoring

☑ RECOMMENDATIONS

Monitoring

- For all patients taking medical cannabis, clinicians should perform an annual assessment for CUD to identify problematic use. (B*) Assessment tools include the CUDIT-R and the DSM-5 criteria.
  - If CUD is diagnosed, clinicians should work with the patient to develop an individualized treatment plan that maximizes benefits and minimizes harm. The plan may include referral to treatment, cannabis cessation, or harm reduction approaches. (A3)
- If a patient experiences new or worsening signs or symptoms of a psychiatric disorder while taking medical cannabis, the clinician should discontinue medical cannabis certification and consult with a psychiatrist or refer the patient for psychiatric assessment and treatment. (A2)
- Clinicians should ask patients about any symptoms of hyperemesis disorder (nausea, vomiting, abdominal pain) and discontinue medical cannabis treatment if the syndrome is identified. (A3)
- If a patient chooses to vape medical cannabis, the clinician should ask about any breathing changes, including reduced exercise tolerance, shortness of breath, or wheezing. (A3)
- If breathing changes occur, the clinician should:
  - Advise the patient to avoid products purchased outside of registered facilities. (A*)
  - Encourage the patient to switch to an administration method other than vaping and advise against future use of inhaled cannabis. (A3)
- If a patient wants to stop using medical cannabis, the clinician should:
  - Inform the patient that cessation of chronic use may result in cannabis withdrawal symptoms, such as irritability, negative mood, nausea, and stomach pain. (A3)
  - Help the patient develop a plan to taper the dose and ultimately discontinue cannabinoid use. (A3)

Abbreviations: CUD, cannabis use disorder; CUDIT-R, Cannabis Use Disorder Identification Test-Revised; DSM, Diagnostic and Statistical Manual of Mental Disorders.

At follow-up appointments, clinicians should ask patients about symptoms of potential adverse effects. Care providers should collaborate with patients' existing treatment teams, including primary care providers, mental health care providers, cardiologists, and other specialists, to monitor these signs and symptoms. The most common adverse effects are described below.

In addition, clinicians should perform an annual assessment for CUD in all patients taking medical cannabis. If CUD is identified, clinicians should engage patients in shared decision-making to revise treatment goals as needed and develop a revised treatment plan to meet the new goals. The treatment plan should prioritize harm reduction and may include increased visits, using methods other than smoking, THC dose reduction, a modified dosing schedule, or linking patients to therapists or other mental health professionals [Fischer, et al. 2017].

Psychiatric symptoms: Chronic cannabis use is associated with psychiatric symptoms, including anxiety, depression, and psychosis, and has been linked to worsening schizophrenia in individuals with a preexisting genetic vulnerability [Di Forti, et al. 2014; Caspi, et al. 2005; Patton, et al. 2002]. However, a direct causal relationship is difficult to establish because multiple confounding factors blur the relationship between cannabis use and psychiatric illness. For example, individuals with anxiety or stress may be more likely to use cannabis [Volkow, et al. 2014]. Care providers should monitor patients for new or worsening psychiatric symptoms and discontinue medical cannabis if symptoms are identified. To decertify patients for medical cannabis use, see New York State Medical Cannabis Program Patient Certification Instructions.

Cannabis hyperemesis syndrome: A recent study reported that gastrointestinal symptoms were the most common cause for emergency room visits related to cannabis use [Monte, et al. 2019]. The most severe gastrointestinal effect of cannabis use, cannabis hyperemesis syndrome [Allen, et al. 2004], manifests as cyclical nausea and vomiting and abdominal pain in individuals with chronic cannabis use. Symptoms may improve with hot showers or baths and resolve after cessation of cannabis use [Schreck, et al. 2018]. Cannabis hyperemesis syndrome has been described primarily in case series as early as 2004 [Venkatesan, et al. 2019; Allen, et al. 2004]; however, the criteria for diagnosing cannabis hyperemesis syndrome have been inconsistent, making it difficult to define the epidemiology. The most recent diagnostic criteria include: 1) episodic vomiting at least 3 times in the past year; 2) cannabis use for at least 1 year; 3) cannabis use at least 4 times per week on average; and 4) resolution of symptoms following a period of abstinence from cannabis use for at least 6 months or a period that spans at least 3 typical cyclical vomiting episodes for the individual [Venkatesan, et al. 2019]. Clinicians should monitor patients using medical cannabis for hyperemesis disorder symptoms; if symptoms are present, a trial of abstinence from cannabis may be appropriate.

Pulmonary effects: For patients who choose to vape, care providers should recommend avoidance of products purchased outside of registered facilities and, during follow-up visits, ask patients about any changes in breathing. Chronic inhaled cannabis use can lead to chronic bronchitis symptoms, including cough, sputum production, and wheezing [Ribeiro and Ind 2018; Tashkin 2018]. Cannabis use may result in pulmonary function test changes, but, unlike tobacco, cannabis has not been associated with chronic obstructive lung disease in observational studies [Ribeiro and Ind 2018; Tashkin 2018]. The mode of consumption could be related to specific types of respiratory syndromes.

A new lung disease associated with heavy vaping emerged in late 2019 [Layden, et al. 2020; Schier, et al. 2019]. To date, it remains unclear whether the risk is limited to specific types of vaping products or oils or with specific use patterns. It is suspected that vaping lung injury is caused by a severe inflammatory response to vitamin E acetate, an oil included in some formulations of vaporized products (including nicotine and cannabinoids). However, more studies are needed to confirm that vitamin E acetate is directly responsible for vaping lung injury [Christiani 2020]. No cases of vaping lung injury have been attributed to New York State medical cannabis vaped products.

Cannabis smoking may predispose individuals to pneumonia through damage of central airways and local immune response changes [Shay, et al. 2003; Baldwin, et al. 1997; Fligiel, et al. 1997].

Smoked cannabis contains carcinogens, raising concerns about lung cancer risk. Observational studies show mixed findings: increased risk of lung cancer in all users of smoked cannabis [Zhang, et al. 2015], only among heavy users [Aldington, et al. 2008], and not at all [Aldington, et al. 2008]. These studies included potential confounders (e.g., tobacco use, environmental exposures) that may have skewed the results. Further research is needed to understand how individuals taking cannabis should be monitored for cancer.

Cognition: Cannabis intoxication has an acute effect on memory and attention, but the effect of cannabis use on long-term cognition has not been well studied [Broyd, et al. 2016; Volkow, et al. 2016]. Some case-control studies found that neuropsychological function was worse in participants who used unregulated cannabis than in controls with no use [Schreiner and Dunn 2012; Grant, et al. 2003]. However, in similar studies of individuals with at least 1 month of abstinence from unregulated cannabis, neuropsychological measures were similar in both groups [Schreiner and Dunn 2012; Grant, et al. 2003]. These findings suggest that any cognitive impairment due to cannabis use may be inversely

related to the length of abstinence. In addition, longitudinal data from a small cohort of adult patients who use medical cannabis indicate improved executive function after 3 months. Medical cannabis could affect cognition differently than unregulated cannabis [Gruber, et al. 2017]

Among adolescents and young adults, whose brains are still developing, cannabis use is associated with changes in cognitive processes that could affect mental health, propensity toward future substance use disorders, and cognition [Hurd, et al. 2019]. As with adults, cognitive performance improves in adolescents after at least 25 days of abstinence from cannabis use [Hurd, et al. 2019]. There remains much to be understood about cannabis use and the developing brain. For additional information about the effects of cannabis use in adolescents and young adults, see the World Health Organization: The Health and Social Effects of Nonmedical Cannabis Use and the American Academy of Pediatrics: Counseling Parents and Teens About Marijuana Use in the Era of Legalization of Marijuana [Ryan and Ammerman 2017; WHO 2016].

Cessation of medical cannabis: In patients with chronic cannabis use, abrupt cessation may lead to symptoms of cannabis withdrawal, which include, but are not limited to, irritability, anxiety, insomnia, depressed mood, strange dreams, headaches, and stomach pain [Bonnet and Preuss 2017]. Clinicians should inform patients who want to stop using cannabis about the risk of cannabis withdrawal symptoms. Treatment of cannabis withdrawal symptoms is not well studied, but symptoms may be managed with, for instance, zolpidem for insomnia or benzodiazepines for anxiety [Brezing and Levin 2018]. Few data exist on the effects of tapering the cannabis, but individuals may experience fewer withdrawal symptoms with a gradual reduction in dose rather than an abrupt stop. Clinicians should discuss these factors with the patient and, if requested, help develop a tapering plan. To decertify patients for medical cannabis use, see New York State Medical Cannabis Program Patient Certification Instructions.

Appendix: Office of Cannabis Management (OCM) Communications

March 9, 2022

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Office of Cannabis Management

NEW YORK STATE

KATHY HOCHUL	TREMAINE WRIGHT	JESSICA GARCIA	REUBEN MCDANIEL, III	JEN METZGER	ADAM W. PERRY	CHRIS ALEXANDER
Governor	Cannabis Control Board Chair	Board Member	Board Member	Board Member	Board Member	Executive Director

March 9, 2022

Dear Provider,

The purpose of this communication is to share important clinical information and update you about key changes in cannabis policies due to the passage of the Marijuana Regulation and Taxation Act (MRTA), which included the creation of a new law, known as the Cannabis Law. The Cannabis Law established a regulatory framework for cannabis in New York grounded in the principles of public health, social equity, and economic justice. The Cannabis Law established the Office of Cannabis Management (OCM) and a five-member Cannabis Control Board (Board) ultimately responsible for licensing businesses to grow and sell cannabis and cannabinoid hemp in New York State. As a part of the implementation of the Cannabis Law in New York State, the OCM and the Board will also be providing laboratory testing, packaging, and labeling requirements to keep consumers safe.

KEY POLICY & REGULATORY UPDATES:
OCM, together with the Board, will comprehensively regulate adult-use cannabis, medical cannabis, and cannabinoid hemp. Following the guidance of the Cannabis Law, we have already taken significant steps to expand the existing Medical Cannabis Program including:

- Expanding the types of providers who can certify patients for the medical use of cannabis to include anyone who is licensed, registered, or certified by New York State to prescribe controlled substances to humans within the State. For more information on how to become a certifying provider visit https://cannabis.ny.gov/practitioners.
- Adding eligible conditions for treatment. A provider may now certify patients for medical cannabis for any condition at their clinical discretion.
- Allowing certified medical patients and designated caregivers to cultivate medical cannabis at home, once regulations have been formally adopted.

For additional key information, please visit: "What You Need to Know" Fact Sheet

CONSUMER SAFETY CONCERNS:
With the passage and implementation of the Cannabis Law, you may see changing behaviors or receive questions from your patients about cannabis use. Below is some key health related information to know and/or share with patients and caregivers:

- New York continues to see calls to Poison Control about accidental ingestion of unregulated cannabis edibles mistaken for snacks or candy. Cannabis products, especially edibles, should be stored locked- up, out of reach, and out of sight of children and pets.
- Currently, there is no regulated legal marketplace for adult-use cannabis products.

  o Some people may be accessing cannabis products from the illicit marketplace where there is no testing or regulatory oversight. These products may contain unsafe ingredients, contaminants, and byproducts, and may be available in potencies and quantities that can result in accidental overconsumption.

Harriman State Office Building Campus, 1220 Washington Ave., Albany, NY 12207 | 1 (888) 626-5151 | info@ocm.ny.gov | cannabis.ny.gov
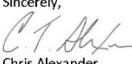
o New and unregulated cannabis products that are different than CBD are also being illegally sold both in retail stores such as smoke shops and online. These include Delta-8 THC, hexahydrocannabinol (HHC), and THC-O-Acetate which can be derived from hemp. Little is known about the safety profile of these novel cannabinoids, and they can pose consumer safety risks. The U.S. Food and Drug Administration released a consumer update cautioning that Delta-8 THC has serious health risks and the OCM does not currently allow the sale of these products. For more information about Delta-8 THC, please visit: FDA Delta-8 THC Information.

o Synthetic cannabinoids, often called K2 and Spice are also available in some retail stores. They contain some plant material treated with synthetic cannabinoids and are unregulated and illegal. Their effects are highly variable and have been associated with dangerous side effects.

- New York continues to see a number of ongoing e-cigarette, or vaping product use-associated lung injury (EVALI) cases. One cause of EVALI is the use of vitamin E acetate, an additive in some THC-containing e-cigarette or vaping products, but there may be other causes. EVALI symptoms can be confused with symptoms of COVID-19. For more information about EVALI, including ICD-10-CM and patient management guidance, please visit: CDC EVALI Guidance. Prompt reporting of cases to Poison Control remains essential.

If you have a patient who has accidentally ingested or has an adverse reaction (including EVALI) that may be due to a novel cannabinoid, a hemp-based product, or any other cannabis product, please call **Poison Control at 1-800-222-1222** and/or connect the patient with the nearest Emergency Department. Any adverse events for patients in the Medical Cannabis Program should be reported to the Person-Based Electronic Response Data System (PERDS) which can be accessed via the Health Commerce System.

Please be assured that the OCM is building a regulated cannabis program that has public health and consumer safety at its core. For more information about key provisions from the MRTA that are intended to protect the public health and safety of New Yorkers, please visit: **The Office of Cannabis Management's Public Health and Safety Fact Sheet.**

OCM will be launching a robust public education campaign in the coming months. Please be on the lookout for additional communications as OCM works to implement the new Cannabis Law. The best way to receive updates in real time is to sign up for OCM updates here. For more information from OCM, please visit https://cannabis.ny.gov/. Questions can be sent to info@ocm.ny.gov.

Sincerely,

Chris Alexander
Executive Director
Office of Cannabis Management

Harriman State Office Building Campus, 1220 Washington Ave., Albany, NY 12207 | 1 (888) 626-5151 | info@ocm.ny.gov | cannabis.ny.gov

All Recommendations

☑ **ALL RECOMMENDATIONS: THEREAPUTIC USE OF MEDICAL CANNABIS IN NEW YORK STATE**

Assessment

- Before approving a patient for medical cannabis use, clinicians should determine the following:
  - Current and previous use of medical, unregulated, and regulated adult-use cannabis, including amount and administration method (A3)
  - Method used for smoking cannabis (e.g., pipe or rolling papers), if applicable (A3)
  - Known history of arrhythmia, CAD, or psychosis (A2)
  - Potential drug-drug interactions with medical cannabis (A*)
- Clinicians should assess and document the qualifying condition for medical cannabis based on medical records and patient evaluation with standardized tools (A*), such as:
  - PEG Scale
  - DSM-5 PTSD Checklist

Medical Cannabis Initiation

- Clinicians should recommend a medical cannabis formulation and dose based on a patient's symptoms and the frequency, amount, and type of cannabis currently in use, if applicable. (A3)
- Clinicians should use caution when recommending medical cannabis to patients with a known history of arrhythmia or CAD, a history of psychosis, or a family history of schizophrenia (A2):
  - For a patient with a history of arrhythmia or CAD, the clinician should determine whether the patient is being treated for the condition and consult the treating care provider. In discussing the risks and benefits of medical cannabis use, clinicians should inform patients that the THC in medical cannabis can elevate heart rate.
  - If a patient has a history of psychosis and is being treated for the condition, the clinician should consult the patient's mental health care provider to determine the context of the psychosis (e.g., substance-induced) and inform the patient that the THC in medical cannabis can exacerbate psychosis.
  - If a patient has active psychosis and is cannabis-naive, the clinician should advise against initiating medical cannabis; if a patient is using unregulated cannabis, the clinician should recommend switching to medical cannabis to reduce THC intake and discuss harm reduction strategies with the patient.
  - If a patient has a family history of schizophrenia, the clinician should inform the patient that cannabis use may precipitate symptoms of schizophrenia.
- Clinicians should counsel patients on the risks and benefits of the available medical cannabis administration methods (see Table 2: Medical Cannabis Administration Methods Currently Available in New York State). (A*)
- Clinicians should advise patients against using vaped or smoked cannabis products. (A*)
- Clinicians should inform patients about potential acute adverse effects of medical cannabis use and provide patient education regarding management of adverse effects (A2):
  - Clinicians should inform patients of the potential for intoxication (i.e., feeling "high"), dizziness, or impairment in concentration; if symptoms occur, recommend that patients lie down and wait for symptoms to resolve and reduce their dose of THC.
  - Clinicians should ensure that patients know to seek emergency medical evaluation if they experience any serious adverse effects, including hallucinations, psychosis, severe anxiety, paranoia, pulmonary or cardiac symptoms, or hyperemesis.
  - Clinicians should inform patients that cannabis use may increase the risk of falls, particularly in elderly individuals.
- Clinicians should inform patients of childbearing potential of the potential risks of using cannabis while pregnant, including preterm labor and intrauterine growth restriction (A2):
  - If a cannabis-naive patient is pregnant, the clinician should advise against initiating any cannabis use.

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- If a pregnant patient is currently using unregulated cannabis, the clinician should first advise against continued use. If the patient plans to continue using cannabis, the clinician should encourage a switch to regulated adult-use or medical cannabis and discuss harm reduction strategies.

- For individuals who could become pregnant, clinicians should recommend the use of contraception while using cannabis.

- Clinicians should inform patients who are <25 years old of the potential for long-term changes in brain development, mental health, and cognition associated with cannabis use in people whose brains are still developing (see guideline section Monitoring > Cognition) (A2):

  - If a cannabis-naive patient is <25 years old, the clinician should advise against initiating cannabis.

  - If a patient <25 years old is currently using unregulated cannabis and intends to continue use, the clinician should advise the patient to switch to regulated adult-use or medical cannabis and discuss harm reduction strategies.

- Clinicians should advise patients to take the first dose of medical cannabis before bedtime and at home in a safe environment to limit potential immediate adverse effects. (A3)

- Clinicians should caution patients about the potential for impaired driving while taking cannabis and advise them to avoid driving or operating heavy machinery while using medical cannabis. (A2)

- Clinicians should inform patients of the risks associated with unregulated cannabis and recommend discontinuation after medical cannabis is initiated. (A3)

Monitoring

- For all patients taking medical cannabis, clinicians should perform an annual assessment for CUD to identify problematic use. (B*) Assessment tools include the CUDIT-R and the DSM-5 criteria.

  - If CUD is diagnosed, clinicians should work with the patient to develop an individualized treatment plan that maximizes benefits and minimizes harm. The plan may include referral to treatment, cannabis cessation, or harm reduction approaches. (A3)

- If a patient experiences new or worsening signs or symptoms of a psychiatric disorder while taking medical cannabis, the clinician should discontinue medical cannabis certification and consult with a psychiatrist or refer the patient for psychiatric assessment and treatment. (A2)

- Clinicians should ask patients about any symptoms of hyperemesis disorder (nausea, vomiting, abdominal pain) and discontinue medical cannabis treatment if the syndrome is identified. (A3)

- If a patient chooses to vape medical cannabis, the clinician should ask about any breathing changes, including reduced exercise tolerance, shortness of breath, or wheezing. (A3)

- If breathing changes occur, the clinician should:

  - Advise the patient to avoid products purchased outside of registered facilities. (A*)

  - Encourage the patient to switch to an administration method other than vaping and advise against future use of inhaled cannabis. (A3)

- If a patient wants to stop using medical cannabis, the clinician should:

  - Inform the patient that cessation of chronic use may result in cannabis withdrawal symptoms, such as irritability, negative mood, nausea, and stomach pain. (A3)

  - Help the patient develop a plan to taper the dose and ultimately discontinue cannabinoid use. (A3)

Abbreviations: CAD, coronary artery disease; CUD, cannabis use disorder; CUDIT-R, Cannabis Use Disorder Identification Test-Revised; DSM, Diagnostic and Statistical Manual of Mental Disorders; PEG, Pain, Enjoyment of Life, and General Activity; THC, delta-9-tetrahydrocannabinol.

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Supplement: Guideline Development and Recommendation Ratings

Table S1: Guideline Development: New York State Department of Health AIDS Institute Clinical Guidelines Program	
Developer	New York State Department of Health AIDS Institute (NYSDOH AI) Clinical Guidelines Program
Funding source	NYSDOH AI
Program manager	Clinical Guidelines Program, Johns Hopkins University School of Medicine, Division of Infectious Diseases. See Program Leadership and Staff.
Mission	To produce and disseminate evidence-based, state-of-the-art clinical practice guidelines that establish uniform standards of care for practitioners who provide prevention or treatment of HIV, viral hepatitis, other sexually transmitted infections, and substance use disorders for adults throughout New York State in the wide array of settings in which those services are delivered.
Expert committees	The NYSDOH AI Medical Director invites and appoints committees of clinical and public health experts from throughout New York State to ensure that the guidelines are practical, immediately applicable, and meet the needs of care providers and stakeholders in all major regions of New York State, all relevant clinical practice settings, key New York State agencies, and community service organizations.
Committee structure	• Leadership: AI-appointed chair, vice chair(s), chair emeritus, clinical specialist(s), JHU Guidelines Program Director, AI Medical Director, AI Clinical Consultant, AVAC community advisor • Contributing members • Guideline writing groups: Lead author, coauthors if applicable, and all committee leaders
Disclosure and management of conflicts of interest	• Annual disclosure of financial relationships with commercial entities for the 12 months prior and upcoming is required of all individuals who work with the guidelines program, and includes disclosure for partners or spouses and primary professional affiliation. • The NYSDOH AI assesses all reported financial relationships to determine the potential for undue influence on guideline recommendations and, when indicated, denies participation in the program or formulates a plan to manage potential conflicts. Disclosures are listed for each committee member.
Evidence collection and review	• Literature search and review strategy is defined by the guideline lead author based on the defined scope of a new guideline or update. • A comprehensive literature search and review is conducted for a new guideline or an extensive update using PubMed, other pertinent databases of peer-reviewed literature, and relevant conference abstracts to establish the evidence base for guideline recommendations. • A targeted search and review to identify recently published evidence is conducted for guidelines published within the previous 3 years. • Title, abstract, and article reviews are performed by the lead author. The JHU editorial team collates evidence and creates and maintains an evidence table for each guideline.

Table S1: Guideline Development: New York State Department of Health AIDS Institute Clinical Guidelines Program	
Recommendation development	• The lead author drafts recommendations to address the defined scope of the guideline based on available published data. • Writing group members review the draft recommendations and evidence and deliberate to revise, refine, and reach consensus on all recommendations. • When published data are not available, support for a recommendation may be based on the committee's expert opinion. • The writing group assigns a 2-part rating to each recommendation to indicate the strength of the recommendation and quality of the supporting evidence. The group reviews the evidence, deliberates, and may revise recommendations when required to reach consensus.
Review and approval process	• Following writing group approval, draft guidelines are reviewed by all contributors, program liaisons, and a volunteer reviewer from the AI Community Advisory Committee. • Recommendations must be approved by two-thirds of the full committee. If necessary to achieve consensus, the full committee is invited to deliberate, review the evidence, and revise recommendations. • Final approval by the committee chair and the NYSDOH AI Medical Director is required for publication.
External reviews	• External review of each guideline is invited at the developer's discretion. • External reviewers recognized for their experience and expertise review guidelines for accuracy, balance, clarity, and practicality and provide feedback.
Update process	• JHU editorial staff ensure that each guideline is reviewed and determined to be current upon the 3-year anniversary of publication; guidelines that provide clinical recommendations in rapidly changing areas of practice may be reviewed annually. Published literature is surveilled to identify new evidence that may prompt changes to existing recommendations or development of new recommendations. • If changes in the standard of care, newly published studies, new drug approval, new drug-related warning, or a public health emergency indicate the need for immediate change to published guidelines, committee leadership will make recommendations and immediate updates and will invite full committee review as indicated.

Table S2: Recommendation Ratings and Definitions		
Strength	**Quality of Evidence**	
A: Strong B. Moderate C: Optional	1	Based on published results of at least 1 randomized clinical trial with clinical outcomes or validated laboratory endpoints.
	*	Based on either a self-evident conclusion; conclusive, published, in vitro data; or well-established practice that cannot be tested because ethics would preclude a clinical trial.
	2	Based on published results of at least 1 well-designed, nonrandomized clinical trial or observational cohort study with long-term clinical outcomes.
	2†	Extrapolated from published results of well-designed studies (including nonrandomized clinical trials) conducted in populations other than those specifically addressed by a recommendation. The source(s) of the extrapolated evidence and the rationale for the extrapolation are provided in the guideline text. One example would be results of studies conducted predominantly in a subpopulation (e.g., one gender) that the committee determines to be generalizable to the population under consideration in the guideline.
	3	Based on committee expert opinion, with rationale provided in the guideline text.