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APPROACHES TO CANNABIS USE DISORDER MEDICATION-ASSISTED TREATMENT GUIDELINE

SCOPE: This Approach to Cannabis Use Disorder Medication-Assisted Treatment (CUD MAT) Guideline is intended to offer prescribing assistance for providers, clients, and the interested general public to increase the effectiveness and utilization of CUD MAT in the ambulatory care setting. It is not intended to be comprehensive in scope. These recommendations are not a substitute for clinical judgment, and decisions about care must carefully consider and incorporate the clinical characteristics and circumstances of each individual client

INTRODUCTION: Cannabis is derived from plants in the Cannabaceae family that include the species *Cannabis sativa* and *Cannabis indica*. The main active chemicals are delta-9 tetrahydro-cannabinol (THC) and cannabidiol (CBD) and their potencies and relative concentrations range widely between preparations. Marijuana is a common form of cannabis and is made from the dried flowers of the cannabis plant. Cannabis is the most commonly used illicit drug in the United States. While cannabis continues to be illegal at the federal level, 19 states and D.C. have legalized recreational use in adults over 21 years of age, and 37 states and D.C. have legalized medical cannabis. In the 2020 National Survey on Drug Use and Health (NSDUH), only approximately one-fourth of people (27.4%) aged 12 or older indicated they perceived that weekly cannabis use as risk for great harm.

While this lower-risk perception of the majority is supported by research, there are in fact potential harms to be kept in mind. For example, in a 2017 National Academy of Sciences, Engineering, and Medicine report there is substantial evidence of a statistical association between cannabis smoking and worse respiratory symptoms in long term adult smokers, increased risk of motor vehicle crashes, lower birthweight in offspring of maternal smokers, and the development of schizophrenia or other psychoses in adolescents. Another potential risk is Cannabinoid Hyperemesis Syndrome (CHS), characterized by chronic cannabis use, cyclic episodes of nausea/vomiting and frequent hot bathing to relieve these symptoms. CHS often requires emergency care. As with almost every substance with use disorder potential, earlier age of use onset is associated with the development of problem use later in life.

With many US and Canadian jurisdictions moving towards legalized/regulated cannabis use, evidence-based "Lower Risk Cannabis Use Guidelines" (LRCUG) have emerged to reduce modifiable risk factors of cannabis-related adverse health outcomes. In general, current evidence suggests that individuals can substantially reduce their risk for adverse health outcomes if they delay the onset of cannabis use until after adolescence, avoid the use of high-potency (i.e. THC)

cannabis products and high-frequency/-intensity of use, and refrain from smoking-routes for administration (see Appendix I).

Cannabis use disorder (CUD) occurs when recurrent use of cannabis leads to significant impairment. The NSDUH survey in 2020 indicated that approximately 1.0 million people (4.1%) aged 12 to 17, 4.5 million people (13.5%) aged 18 to 25, and 8.7 million people (4.0%) aged 26 or older had a CUD. A range of interventions should be considered for all people with CUD including assessment and management of withdrawal and long-term strategies to reduce the medical and psychosocial harms of CUD. In addition, any co-occurring conditions that jeopardize a person's treatment success should be addressed.

ASSESSMENT AND INTERVENTION PLANNING:

As with any substance with abuse potential, the DSM-5-TR details diagnostic criteria for CUD (specifiers: in early remission, in sustained remission, in a controlled environment, mild, moderate, severe) in addition to cannabis intoxication (specifier: with perceptual disturbances), cannabis withdrawal, other cannabis-induced disorders, and unspecified cannabis-related disorder. To meet criteria for CUD, clients must exhibit at least 2 out of 11 DSM-5-TR criteria over a 12-month period leading to clinically significant impairment and/or distress. Examples of these criteria include: using cannabis in larger amounts over a longer period of time than intended, use in hazardous situations, cravings for cannabis, and experiencing tolerance and/or withdrawal, among others. The severity of the use disorder is based on the number of criteria met with mild use disorder associated with 2-3, moderate use disorder associated with 4-5, and severe use disorder associated with 6 or more criteria met. There is strong evidence that frequency of cannabis use as well as younger age of first use are associated with higher severity CUD. Several tools varying in length have been developed to assist in screening, assessing, and monitoring CUD. For example, the Cannabis Abuse Screening Test (CAST, appendix II) is a 5-item, 15-point screen that has been validated for use in adolescents and young adults. The Cannabis Use Problems Identification Test (CUPIT©) is a 16-item, 82-point instrument validated for use in adolescents and adults.

There are associations between mental health problems contributing to cannabis use as well as cannabis use contributing to mental health problems. Therefore, it may be useful for specialty mental health evaluation anytime along the course of treatment for a client with CUD. Active use and active withdrawal complicate evaluation and/or treatment of underlying primary mental health diagnoses. Currently, more work is needed to develop evidence-based approaches to the pharmacological management of individuals with comorbid CUD and other mental health diagnoses.

WITHDRAWAL AND MANAGEMENT: After heavy or prolonged cannabis use, cessation can lead to clinically significant impairment or distress due to a withdrawal syndrome that can include:

1. Irritability, anger, or aggression
2. Nervousness or anxiety
3. Sleep difficulty (e.g. insomnia, disturbing dreams)
4. Decreased appetite or weight loss

5. Restlessness
6. Depressed mood
7. At least one of the following physical symptoms causing significant discomfort: abdominal pain, shakiness/tremors, sweating, fever, chills, or headache

Individual withdrawal symptoms have their own time course but generally withdrawal symptoms begin a day or two after abstinence and can last about two weeks. Higher levels of dependence are associated with higher levels of withdrawal after cannabis cessation. The Cannabis Withdrawal Scale (CWS, Appendix III) is a 19-item measure that has been validated for use in both clinical and research settings to assess the severity of cannabis withdrawal. Higher withdrawal severity is correlated with a higher degree of functional impairment in normal daily activities as well as the propensity for relapse to cannabis use.

While withdrawal symptoms contribute to functional impairment and propensity for relapse during the withdrawal period, the role of pharmacological management of withdrawal symptoms is not clear. Generally low-quality studies have shown some benefit on cannabis withdrawal sleep difficulties for gabapentin, lofexidine, mirtazapine, quetiapine, and zolpidem, however further, higher quality studies are needed to confirm the utility of these medications (Refer to Community Behavioral Health Services guidelines for prescribing information). Cannabinoid replacement/modulation strategies with dronabinol (THC), nabilone (synthetic THC derivative), nabiximols (THC and CBD combination), and CBD have sometimes demonstrated positive effects on reducing cravings and withdrawal symptoms (see below for more information).

CUD OFF-LABEL PHARMACOTHERAPY: Clinical trials have not shown consistent evidence of efficacy for any medication in the treatment of CUD; no medication is approved for this indication by the US Food and Drug Administration. Every study investigating medication for CUD reviewed here included psychosocial interventions and as such medication treatment alone is not recommended. Gabapentin, N-acetylcysteine (NAC), topiramate, and varenicline have yielded the most favorable results in clinical trials in reducing cannabis use. Trials with antidepressants have shown they decrease cannabis abstinence rates while having no effects on decreasing use or withdrawal symptoms. Trials with other medications including antipsychotics, anxiolytics, mood stabilizers, cognitive enhancers, anticonvulsants, antiemetics, and oxytocin have shown mixed or negative findings.

GABAPENTIN: Gabapentin is a GABAergic agent that binds to receptors with GABA-like activity modulating release of excitatory neurotransmitters. The exact mechanism to aid in treatment of CUD is not known. In one clinical trial, gabapentin in addition to psychosocial intervention led to short-term reduction in cannabis use compared to placebo. See Appendix IV for dosing recommendations and client considerations.

Side effects: Common side effects include dizziness, drowsiness, ataxia, nausea, vomiting, and tremor.

Drug interactions: There are no clinically meaningful drug interactions with gabapentin. Side effects may be enhanced when combined with other CNS depressant medications and substances. There is increasing concern for gabapentin contributing to overdose deaths in recent years given the increasing rates of prescribing of this agent.

N-ACETYLCYSTEINE (NAC): NAC is an N-acetyl prodrug of the naturally occurring amino acid cysteine. It is an agent typically used for acetaminophen overdose in its intravenous form or as a mucolytic in its inhaled form but has been tested orally in the treatment of CUD. Oral NAC is available over-the-counter as a dietary supplement. While there are RCTs demonstrating NAC with Contingency Management in addition to other psychosocial interventions as effective in reducing cannabis intake in treatment seeking subjects, a recent systematic review of the 8 RCTs of NAC for CUD concluded that it was premature to conclude that there is a strong level of evidence for its efficacy. Given NAC's low risk potential and some evidence for efficacy, it still may be worthwhile trialing in certain clients with CUD (i.e. adolescents). See Appendix IV for dosing recommendations and client considerations.

Side effects: When given orally, side effects can include mild nausea, stomach upset, and vomiting. When used in trials, NAC was generally well tolerated.

Drug interactions: There are no clinically meaningful drug interactions with N-acetylcysteine.

TOPIRAMATE: Topiramate is an antiepileptic targeting several membrane ion channels and neurotransmitter receptors. In one study of adolescents and adults, topiramate plus psychosocial intervention did not decrease percent use days but may have decreased grams used per day at the end of the study as there was a statistical trend towards this. The topiramate group had higher dropout rates compared to placebo due to adverse events. See Appendix IV for dosing recommendations and client considerations.

Side effects: Paresthesias, taste perversion, anorexia and weight loss, diarrhea, fatigue and drowsiness, impaired concentration, uncommon but serious metabolic acidosis.

Drug interactions: By virtue of its anticholinergic activity, topiramate has multiple drug interactions with other agents with anticholinergic activity increasing the risk of non-exertional hyperthermia. Caution is advised with polypharmacy.

VARENICLINE: Varenicline is a selective nicotinic receptor partial agonist approved for smoking cessation. In one underpowered pilot RCT, varenicline decreased self-reported cannabis use and urine cannabinoid levels. See Appendix IV for dosing recommendations and client considerations.

Side effects: The most common side-effect associated with varenicline is nausea and other common side effects include headache, difficulty sleeping and abnormal dreams. Varenicline carried a boxed warning regarding potential neuropsychiatric side effects that was removed in 2016 after more recent studies demonstrated no difference in neuropsychiatric side effects compared with nicotine or bupropion. Neuropsychiatric effects include behavioral changes, hostility, agitation, depressed mood, and suicidal thoughts and attempts. Systematic reviews of varenicline in clients with mental health disorders reveal no significant difference in neuropsychiatric events compared to placebo, however the included studies have smaller sample sizes and exclude clients with unstable psychiatric symptoms. Despite the removal of the warning, clients should be counseled on the potential exacerbation of psychiatric symptoms and

report any changes in mood or behavior. In the event of new or worsening suicidal thoughts, varenicline should be stopped immediately.

Drug interactions: There are no known major drug interactions with varenicline.

DRONABINOL: Dronabinol (THC) is a CB1 receptor agonist and in one study was found to decrease cannabis withdrawal symptoms and increase treatment retention without having effects on cannabis use or abstinence compared to placebo. See Appendix IV for dosing recommendations and client considerations.

Side effects: More common side effects include clumsiness or unsteadiness, dizziness, drowsiness, false sense of well-being, nausea, trouble with thinking, and vomiting. Hallucinations and delusions have also been reported so dronabinol should be avoided in those at risk for psychosis.

Drug interactions: See Appendix V.

NABIXIMOLS: Nabiximols are a combination of THC and CBD. Studies show mixed results on decreasing cannabis use, withdrawal symptoms and cravings. Nabiximols are not currently available in the US.

Side effects: Common side effects include dizziness, drowsiness, constipation or diarrhea, fatigue, memory or concentration problems, and a dry mouth or changed sense of taste. Hallucinations and delusions have been reported and nabiximols should be avoided in those at risk for psychosis.

Drug interactions: See Appendix V.

CANNABIDIOL: CBD is a CB2 receptor agonist, a CB1 receptor partial antagonist, and inhibits endocannabinoid hydrolysis and reuptake. In one study it was shown to have dose dependent positive effects on cannabis use and abstinence, and withdrawal symptoms and craving and treatment retention were not measured in this study. See Appendix IV for dosing recommendations and client considerations.

Side effects: CBD can cause side effects such as dry mouth, diarrhea, reduced appetite, drowsiness and fatigue.

Drug interactions: See Appendix V.

DURATION OF TREATMENT WITH CUD PHARMACOTHERAPY: Clinical trials for CUD ranged in duration from 4-12 weeks, with unmedicated follow up at 24 weeks. There are no long-term or discontinuation trials, therefore the optimal duration of CUD medication treatment and termination strategies have not been established

CANNABINOID DRUG INTERACTIONS:

THC and CBD are two pharmacologically active cannabinoids found in marijuana. Both may contribute to potential pharmacokinetic drug-drug interactions involving cytochrome P450 (CYP) enzymes responsible for drug metabolism (see Appendix V). Pharmacodynamic interactions may also be seen when marijuana is used concomitantly with other medications.

SPECIAL POPULATIONS:

Pregnancy: The American College of Obstetricians and Gynecologists (ACOG), the American Academy of Pediatrics (AAP), and the Academy of Breastfeeding Medicine advise avoiding cannabis use during pregnancy due to concerns for the neurodevelopmental impact on the fetus. Chemical products from cannabis use are transferred across the placenta.

Gabapentin crosses the placenta and adverse effects have been observed in animal reproduction studies, however pregnancy registry outcome data following maternal use of gabapentin during pregnancy is limited. Folic acid supplementation is recommended prior to and during pregnancy in women using gabapentin.

With NAC use, adverse events have not been observed in animal reproduction studies. Based on limited reports using NAC to treat acetaminophen overdose in pregnant women, NAC has been shown to cross the placenta.

Topiramate should be avoided in those who are pregnant or may become pregnant due to risk of teratogenicity.

For varenicline there is inadequate human data available to assess risk to fetus but there is some animal data indicating potential for decreased fetal weight.

Both dronabinol and cannabidiol should be avoided in pregnancy.

Lactation: Cannabis is transferred into breast milk and may be present up to 6 days after maternal use.

Gabapentin is present in breast milk. The decision to breastfeed during therapy should consider the risk of infant exposure, the benefits of breastfeeding to the infant, and benefits of treatment to the mother. The potential risks of exposure for the infant include drowsiness, inadequate weight gain, and delay in developmental milestones.

It is not known if NAC is excreted in breast milk and the decision to continue or discontinue breast-feeding during therapy should consider the risk of infant exposure, the benefits of breast-feeding to the infant, and benefits of treatment to the mother.

Limited data suggests that maternal topiramate generally result in low levels in infant serum however diarrhea and sedation have been reported on occasion.

There is no human data available to assess risk to infant for breast-feeding mothers taking varenicline so mothers who chose to take varenicline while breastfeeding should monitor their infants for seizures and abnormal vomiting.

There is very little to no human data assessing risk to infants or on milk production for dronabinol (some indication of potential delayed psychomotor development for infant) or cannabidiol so these should be avoided during breast feeding.

Adolescents: Only NAC, topiramate, and cannabidiol have been studied in teenagers under 18 years of age and therefore these agents should be considered first for MAT for CUD in this population.

PSYCHOSOCIAL THERAPIES:

A 2016 Cochrane review looked at the efficacy of various psychosocial interventions for the treatment of CUD in the ambulatory setting. The selection included 23 randomized controlled studies involving 4045 participants from the United States, Australia, Switzerland, Canada, Brazil, and Ireland. While the generalizability of the findings were limited due to the homogeneous nature of the treatment seekers in each locality and other study limitations, psychosocial intervention, in comparison with minimal treatment controls, reduced the frequency of use and severity of dependence in the short-term.

The strongest evidence of efficacy for the use of psychosocial interventions was for cognitive-behavioral therapy (CBT), motivational enhancement therapy (MET), and their combination, provided in more than four sessions delivered over a period of four to six months. Contingency management (CM) interventions were found to contribute to improvements in CUD when combined with CBT or MET + CBT. MET may be particularly useful when working with individuals with lower motivation to change their cannabis use who are just beginning treatment. These interpretations of the treatment literature remain valid through Dec 2021 according to an UpToDate article “Cannabis Use disorder in adults” that includes more recent studies.

We recommend the use of psychopharmacological interventions as an adjunct to structured behavioral and motivational enhancing therapies. The interventions utilized will be based on client preference and actual treatment availability. Please see Appendix VI for other psychosocial resources and supports.

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Appendix I: Abridged from Fischer B., Robinson T., Bullen C., et al "Lower-Risk Cannabis Use Guidelines (LRCUG) for reducing health harms from non-medical cannabis use: A comprehensive evidence and recommendations update," Int J. of Drug Policy, 99 (2022)

Textbox 1. The LRCUG' Recommendations

General Precaution A: People who use cannabis (PWUC) need to know that there is no universally safe level of cannabis use; thus, the only reliable way to avoid any risk for harm from using cannabis is to abstain from its use.

[Evidence Grade: Conclusive]

Recommendation #1: The initiation of cannabis use should be delayed until after late adolescence, or the completion of puberty, to reduce development-related vulnerabilities for harm.

[Evidence Grade: Moderate]

Recommendation #2: PWUC should use 'low-potency' cannabis products, i.e., cannabis products with ideally lower total THC content, or a high CBD/THC content ratio.

[Evidence Grade: Substantial to Moderate]

Recommendation #3: All main available modes-of-use options come with some risk for harm; PWUC should refrain from cannabis 'smoking' and employ alternative routes-of-use for pulmonary health protection.

[Evidence: Substantial to Moderate]

Recommendation #4: If use occurs by inhalation, PWUC should avoid "deep inhalation", prolonged breath-holding, or similar inhalation practices.

[Evidence Grade: Limited]

Recommendation #5: PWUC should refrain from frequent (e.g., daily or near-daily) or intensive (e.g., binging) cannabis use, and instead limit themselves to less frequent or occasional use.

[Evidence Grade: Substantial]

Recommendation #6: Where circumstances allow, PWUC should use legal and quality-controlled cannabis products and use devices.

[Evidence grade: Limited]

Recommendation #7: PWUC who experience impaired cognitive performance should consider temporarily suspending or substantially reducing the intensity (e.g., frequency/potency) of their cannabis use.

[Evidence: Limited]

Recommendation #8: PWUC should avoid driving a motor-vehicle or operating machinery while under the influence of cannabis because of acute impairment and elevated risk of crash involvement, including injury or death; however, the severity and duration of impairment vary depending on multiple factors.

[Evidence Grade: Substantial to Moderate]

Recommendation #9: It is prudent for people who intend to procreate and for women who are pregnant or breastfeeding to abstain from cannabis use towards reducing possible risks for reproduction and of health harm to offspring, respectively.

[Evidence Grade: Limited]

Recommendation #10: PWUC should exercise general caution in combining other psychoactive substances with cannabis use.

[Evidence Grade: Moderate to Limited]

APPENDIX II: CANNABIS ABUSE SCREENING TEST

In the last 12 months, have you smoked cannabis?
Yes □ No □

In the last 12 months…	Never	Rarely	From time to time	Fairly often	Very often
Have you smoked cannabis before midday?	□ 0	□ 1	□ 2	□ 3	□ 4
Have you smoked cannabis when you were alone?	□ 0	□ 1	□ 2	□ 3	□ 4
Have you had memory problems when you smoked cannabis?	□ 0	□ 1	□ 2	□ 3	□ 4
Have friends or members of your family told you that you ought to reduce your cannabis use?	□ 0	□ 1	□ 2	□ 3	□ 4
Have you tried to reduce or stop your cannabis use without succeeding?	□ 0	□ 1	□ 2	□ 3	□ 4
Have you had problems because of your use of cannabis (argument, fight, accident, bad result at school, etc)?	□ 0	□ 1	□ 2	□ 3	□ 4
Which ones?					

To calculate a score, the responses are coded on a scale of 0 to 4. The total score obtained (which can range from 0 to 24) indicates if the questioned users are at risk. A score of less than 3 indicates no addiction risk. A score of 3 or less than 7 indicates low addiction risk, and a score of 7 or above indicates high addiction risk.

SCORE	

APPENDIX III: CANNABIS WITHDRAWAL SCALE

Instructions: This version of the CWS asks about symptoms experienced over the last 24 hours, and can be administered by an interviewer OR by self-report.

The following statements describe how you have felt over the last 24 hours. Please **circle the number** that most closely represents your personal experiences for each statement. For each statement, please rate its negative impact on normal daily activities on the same scale (0 = Not at all to 10 = Extremely), writing the number in the right-hand column.

	Not at all					Moderately						Extremely	Negative Impact on daily activity (0 – 10)
1	The only thing I could think about was smoking some cannabis	0	1	2	3	4	5	6	7	8	9	10	
2	I had a headache	0	1	2	3	4	5	6	7	8	9	10	
3	I had no appetite	0	1	2	3	4	5	6	7	8	9	10	
4	I felt nauseous (like vomiting)	0	1	2	3	4	5	6	7	8	9	10	
5	I felt nervous	0	1	2	3	4	5	6	7	8	9	10	
6	I had some angry outbursts	0	1	2	3	4	5	6	7	8	9	10	
7	I had mood swings	0	1	2	3	4	5	6	7	8	9	10	
8	I felt depressed	0	1	2	3	4	5	6	7	8	9	10	
9	I was easily irritated	0	1	2	3	4	5	6	7	8	9	10	
10	I had been imagining being stoned	0	1	2	3	4	5	6	7	8	9	10	
11	I felt restless	0	1	2	3	4	5	6	7	8	9	10	
12	I woke up early	0	1	2	3	4	5	6	7	8	9	10	
13	I had a stomach ache	0	1	2	3	4	5	6	7	8	9	10	
14	I had nightmares and/or strange dreams	0	1	2	3	4	5	6	7	8	9	10	
15	Life seemed like an uphill struggle	0	1	2	3	4	5	6	7	8	9	10	
16	I woke up sweating at night	0	1	2	3	4	5	6	7	8	9	10	
17	I had trouble getting to sleep at night	0	1	2	3	4	5	6	7	8	9	10	
18	I felt physically tense	0	1	2	3	4	5	6	7	8	9	10	
19	I had hot flashes	0	1	2	3	4	5	6	7	8	9	10	

APPENDIX IV: OFF-LABEL CUD MEDICATION ASSISTED TREATMENT

Product	Dosage	Common Side Effects	Renal Dosing	Hepatic Dosing	Monitoring
Gabapentin 100mg, 300mg, 400mg capsules 600mg, 800mg tablets 250mg/5ml oral solution	Day 1 300mg qHS Day 2 300 mg BID Day 3 300 mg TID Day 4: 300 mg qAM and qMiday and 600mg qEvening (target). Subjects maintained the 1200 mg/day dose until week 11.	Dizziness, drowsiness, ataxia, peripheral edema, abnormal gait, confusion, weight gain, nausea, diarrhea, xerostomia, tremor, nystagmus.	CrCl 30-59ml/min: 200 to 700mg BID CrCl 16-29ml/min: 200 to 700mg daily CrCl 15ml/min: 100 to 300mg daily CrCl <15ml/min: reduce daily dose in proportion to CrCl based on dose for CrCl of 15 ml/min.	No adjustment necessary.	Cr at baseline.
N-acetylcysteine OTC: 600mg capsules	1200mg BID	Mild nausea, stomach upset, and vomiting.	No adjustments necessary.	No adjustments necessary.	None.
Topiramate 15mg, 50mg, 100mg, 200mg tablets	Days 1-7 25mg daily Days 8-14 50mg daily Days 15-17 75mg daily Days 18-21 100mg daily Days 22-24 125mg daily Days 25-28 150mg daily Days 29-42 200mg daily (target) Days 43-44 100mg daily (taper) Days 45-46 50mg daily (taper) Day 45 0mg (off)	Paresthesias, taste perversion, anorexia and weight loss, diarrhea, fatigue and drowsiness, impaired concentration, uncommon but serious metabolic acidosis.	CrCl <70ml/min decrease dose by 50%.	Not defined, caution advised.	Cr and bicarbonate at baseline.
Varenicline 0.5mg, 1mg tablets	Days 1-3 0.5mg daily Days 4-7 0.5mg BID Days 8-42 1mg BID (target)	Nausea, headache, difficulty sleeping and abnormal dreams,	CrCl <30ml/min start 0.5mg daily, 0.5mg BID max.	No adjustments necessary.	Cr at baseline.

	[Dose reduced to 0.5mg BID for tolerability.]	psychiatric exacerbation.			
Dronabinol 2.5mg, 5mg, 10mg capsules	10mg daily titrated to 20mg BID as tolerated in first week.	Clumsiness or unsteadiness, dizziness, drowsiness, false sense of well-being, nausea, trouble with thinking, and vomiting	Not defined.	Not defined.	Avoid if risk for psychosis.
Cannabidiol 100mg/mL solution	200mg BID Or 400mg BID	Dry mouth, diarrhea, reduced appetite, drowsiness and fatigue	No adjustments necessary.	Child-Pugh Class B: start 1.25mg/kg/dose bid, increase to 2.5-5 mg/kg/dose bid max. Child-Pugh Class C: start 0.5mg/kg/dose bid, increase to 1—2 mg/kg/dose bid max.	AST, ALT, TBili at baseline, 1month, 3month, 6month, then periodically and within 1month of dose changes, concurrent hepatotoxic medication changes, or more frequently if on valproate or elevated baseline LFTs.

APPENDIX V: CANNABINOID DRUG INTERACTIONS.

Cannabinoid levels can be increased by other medications that inhibit CYP metabolism	• THC is metabolized by CYP3A4 and CYP2C9 • Cannabidiol is metabolized by CYP3A4 • CYP3A4 and CYP2C9 inhibitors could augment the psychoactive effects of THC and cannabidiol through prolonged exposure
Cannabinoids can affect the levels of other drugs	• Cannabidiol inhibits CYP2C19 (and possibly CYP3A4/5) • Drugs metabolized by CYP2C19 (e.g., warfarin) could have levels elevated
Smoking marijuana can increase clearance of some drugs	• Smoked marijuana has been reported to increase the clearance of drugs metabolized by CYP1A2 (e.g., theophylline, clozapine, olanzapine) with regular marijuana use (>2 marijuana cigarettes per week) • Increased drug clearance results in decreased drug levels
Additive pharmacodynamic effects can occur with other drugs	• Additive effects can occur when marijuana is combined with sympathomimetics (↑ tachycardia, ↑ hypertension), central nervous system depressants such as alcohol and opioids (↑ sedation, ↑ ataxia), and anticholinergics (↑ tachycardia, ↑ confusion)

APPENDIX VI: LOCAL RESOURCES & INFORMATION:

Program name	Overview
Treatment Access Program (TAP) 1380 Howard St, 1st Floor San Francisco, CA 94103 Phone: (415) 503 – 4730 Hours of Operation: Mon – Fri: 8:00AM – 5:00PM *Accepts walk-in. New intakes until 2:00pm.*	The centralized site within SFDPH BHS that provides substance use disorders screening, assessment, level of care recommendations, and placement authorization for SUD residential treatment. Provides referrals to other SUD programs and provider consultation.
Free Cannabis Use Cessation Groups	
Marijuana Anonymous "Friends Of Bud Group" Park Presidio Methodist Church 4301 Geary Boulevard 1st Floor San Francisco, California 94118 Hours: Tuesday 7:30-8:45pm	A 12-step help program for individuals with problematic cannabis use.
12-Step Programs (MA, NA, AA, Al-Anon, etc) Various dates, time and locations Marijuana Anonymous (MA): https://marijuana-anonymous.org/ LifeRing Secular Recovery: https://lifering.org/	Groups for individuals for whom drug use has become a problem and who meet regularly to help each other stay sober. Narcotics Anonymous (NA): http://sfna.org/ Alcoholics Anonymous (AA): http://www.aasf.org/
Resources for Providers	
Marijuana Lit: A Fact-Based Toolkit for Prevention https://attcnetwork.org/centers/network-coordinating-office/marijuana-lit-infographics	Infographic posters of marijuana effects.
Resources for Clients & Families	
California DPH: Let's Talk Cannabis https://www.cdph.ca.gov/Programs/DO/letstalkcannabis/Pages/LetsTalkCannabis.aspx	The California Department of Public Health provides facts and resources regarding cannabis and how it affects our bodies, minds and health.
NIDA: Cannabis Facts for Teens https://www.drugabuse.gov/sites/default/files/teens_brochure_2013.pdf	Client brochure directed at providing information, FAQs, and resources for adolescents/young adults regarding cannabis use.
[CANNABIS] DECODED https://www.smchealth.org/cannabis	A San Mateo County initiative to educate youth and young adults about the facts on cannabis use.

Truth (or nah?!) SF https://www.truthornahsf.org/	Another resource for youth and adolescents about cannabis use.
Systematically Testing the Evidence on Marijuana https://www.cannabisevidence.org/evidence-syntheses/	Living systematic reviews of potential cannabis medical interventions for clients and providers.
Substance Abuse and Mental Health Services Administration https://www.samhsa.gov/marijuana	Information for clients and families from SAMHSA.