



# VA/DoD CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF SUBSTANCE USE DISORDERS

**Department of Veterans Affairs**

**Department of Defense**

## **Clinician Summary**

### **QUALIFYING STATEMENTS**

The Department of Veterans Affairs and the Department of Defense guidelines are based upon the best information available at the time of publication. They are designed to provide information and assist decision making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.

This Clinical Practice Guideline is based on a systematic review of both clinical and epidemiological evidence. Developed by a panel of multidisciplinary experts, it provides a clear explanation of the logical relationships between various care options and health outcomes while rating both the quality of the evidence and the strength of the recommendation.

Variations in practice will inevitably and appropriately occur when clinicians take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation.

These guidelines are not intended to represent TRICARE policy. Further, inclusion of recommendations for specific testing and/or therapeutic interventions within these guidelines does not guarantee coverage of civilian sector care. Additional information on current TRICARE benefits may be found at [www.tricare.mil](http://www.tricare.mil) or by contacting your regional TRICARE Managed Care Support Contractor.

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## I. Introduction

The Department of Veterans Affairs (VA) and Department of Defense (DoD) Evidence-Based Practice Work Group (EBPWG) was established and first chartered in 2004, with a mission to advise the “...Health Executive Council on the use of clinical and epidemiological evidence to improve the health of the population across the Veterans Health Administration and Military Health System,” by facilitating the development of clinical practice guidelines (CPGs) for the VA and DoD populations.<sup>[1]</sup> This CPG is intended to provide primary care clinicians and other healthcare providers with a framework by which to evaluate, treat, and manage the individual needs and preferences of patients with substance use disorders (SUD), leading to improved clinical outcomes.

In 2009, the VA and DoD published a CPG for the Management of Substance Use Disorders (2009 SUD CPG), which was based on evidence reviewed through January 2007. Since the release of that guideline, a growing body of research has expanded the general knowledge and understanding of SUD. Recognition of the complex nature of this condition has led to the adoption of new strategies to manage and treat patients with SUD, including new developments related to pharmacotherapy and other treatment options.

Consequently, a recommendation to update the 2009 SUD CPG was initiated in 2014. The updated CPG includes objective, evidence-based information on the management of SUD. It is intended to assist healthcare providers in all aspects of patient care, including, but not limited to, diagnosis, treatment, and follow-up. The system-wide goal of evidence-based guidelines is to improve the patient’s health and wellbeing by guiding health providers who are taking care of patients with SUD along the management pathways that are supported by evidence. The expected outcomes of successful implementation of this guideline are to:

- Assess the patient’s condition and determine in collaboration with the patient the best treatment method
- Optimize each individual’s recovery to decrease or eliminate consumption, improve health and wellness, live a self-directed life, and strive to reach his or her full potential <sup>[2]</sup>
- Minimize preventable complications and morbidity
- Emphasize the use of patient-centered care

## II. Scope of this Clinical Practice Guideline

Regardless of setting, any patient in the healthcare system should be offered access to the interventions that are recommended in this guideline after taking into consideration the patient’s specific circumstances.

Guideline recommendations are intended to be patient-centered. Thus, treatment and care should take into account a patient’s needs and preferences. Good communication between healthcare professionals and the patient is essential and should be supported by evidence-based information tailored to the patient’s needs. Use of an empathetic and non-judgmental (versus a confrontational) approach facilitates discussions sensitive to gender, culture, and ethnic differences. The information that patients

are given about treatment and care should be culturally appropriate and available to people with limited literacy skills. It should also be accessible to people with additional needs such as physical, sensory, or learning disabilities. Family involvement should be considered if appropriate.

This CPG is designed to assist providers in managing or co-managing patients with SUD. Moreover, the patient population of interest for this CPG is adults who are eligible for care in the VA and DoD healthcare delivery systems. It includes Veterans as well as deployed and non-deployed Active Duty Service Members. This CPG does not provide recommendations for the management of SUD in children or adolescents.

### **III. Engagement Strategies**

A fundamental goal of this VA/DoD CPG is to promote early engagement and retention of patients with substance use conditions who can benefit from addiction-focused treatment. Provider encouragement and support may improve willingness to pursue further involvement in treatment. Among the principles fundamental to the engagement/re-engagement process for patients with SUD are the following, which are elaborated in the full guideline on page 15:

- Indicate to the patient and significant others that treatment is more effective than no treatment
- Use a motivational interviewing style and emphasize common elements of effective interventions
- Emphasize predictors of successful outcomes
- Use strategies effective in promoting involvement in group mutual help programs
- Coordinate evidence-based interventions for co-occurring conditions
- Provide intervention in the least restrictive setting necessary for safety and effectiveness
- Re-engage patients who drop out of treatment
- Maintain motivational interviewing style of interactions, emphasizing future treatment options for patients currently unwilling to engage in addictions-focused care

### **IV. Patient-centered Care**

VA/DoD CPGs encourage clinicians to use a patient-centered care approach that is individualized based on patient capabilities, needs, goals, prior treatment experience, and preferences. Regardless of setting, all patients should be offered access to appropriate evidence-based interventions. Clinicians should review with the patient the outcomes of previous self-change efforts and past treatment experiences. They should discuss willingness for referral for specialty care and involve the patient in prioritizing problems and setting goals. Care of Veterans and Service Members in transition between facilities, services, or from the DoD healthcare system to the VA healthcare system, should include a transition plan that ensures continuity of care and coordination between providers. Healthcare teams should work jointly to provide assessment, services, and continuity of care to patients within this transitioning population.

## V. Shared Decision Making

Throughout this VA/DoD CPG, the authors encourage clinicians to focus on shared decision making (SDM). The SDM model was introduced in *Crossing the Quality Chasm*, an Institute of Medicine report, in 2001.<sup>[3]</sup> It is readily apparent that patients with SUD, together with their clinicians, make decisions regarding care in which they choose to engage. However, patients require sufficient information to be able to make informed decisions. Clinicians must be adept at presenting information regarding individual treatments to their patients, as well as levels and locations of care. For instance, for a patient who is not interested in specialty referral, the clinician should briefly explore the patient's rationale, present relevant and individualized information about how specialty care might better meet the patient's needs, define reasons a specialty referral might be recommended for his or her specific case, and provide information regarding the abilities and the limitations of the primary care clinic. If the patient continues to decline specialty referral despite counseling, the primary care clinician should respect this decision by providing as much care as possible for the patient. Unfortunately, SDM can be complicated as the patient's ability to make decisions may be impaired by the SUD itself.<sup>[4]</sup>

## VI. Addiction-focused Medical Management

Addiction-focused Medical Management is a manualized psychosocial intervention designed to be delivered by a medical professional (e.g., physician, nurse, physician assistant) in a primary care (or general mental health care) setting.<sup>[5]</sup> The treatment uses an SDM approach and provides strategies to increase medication adherence, as well as monitoring of substance use and consequences. It also supports abstinence through education and referral to support groups. While variably defined, addiction-focused Medical Management typically includes:<sup>[6-10]</sup>

1. Monitoring self-reported use, laboratory markers, and consequences
2. Monitoring adherence, response to treatment, and adverse effects
3. Education about alcohol use disorder (AUD) and opioid use disorder (OUD) consequences and treatments
4. Encouragement to abstain from illicit opioids and other addictive substances
5. Encouragement to attend community supports for recovery (e.g., Alcoholics Anonymous [AA], Narcotics Anonymous [NA], Self-Management and Recovery Training [SMART] Recovery) and make lifestyle changes that support recovery

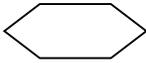
Session structure varies according to the patient's substance use status and treatment compliance. An initial session (40–60 minutes) includes assessment and initial treatment. Subsequent monitoring visits typically last 15 to 25 minutes and occur twice weekly for the first week, tapering to once weekly then once every two weeks for 12 weeks.

## VII. Algorithm

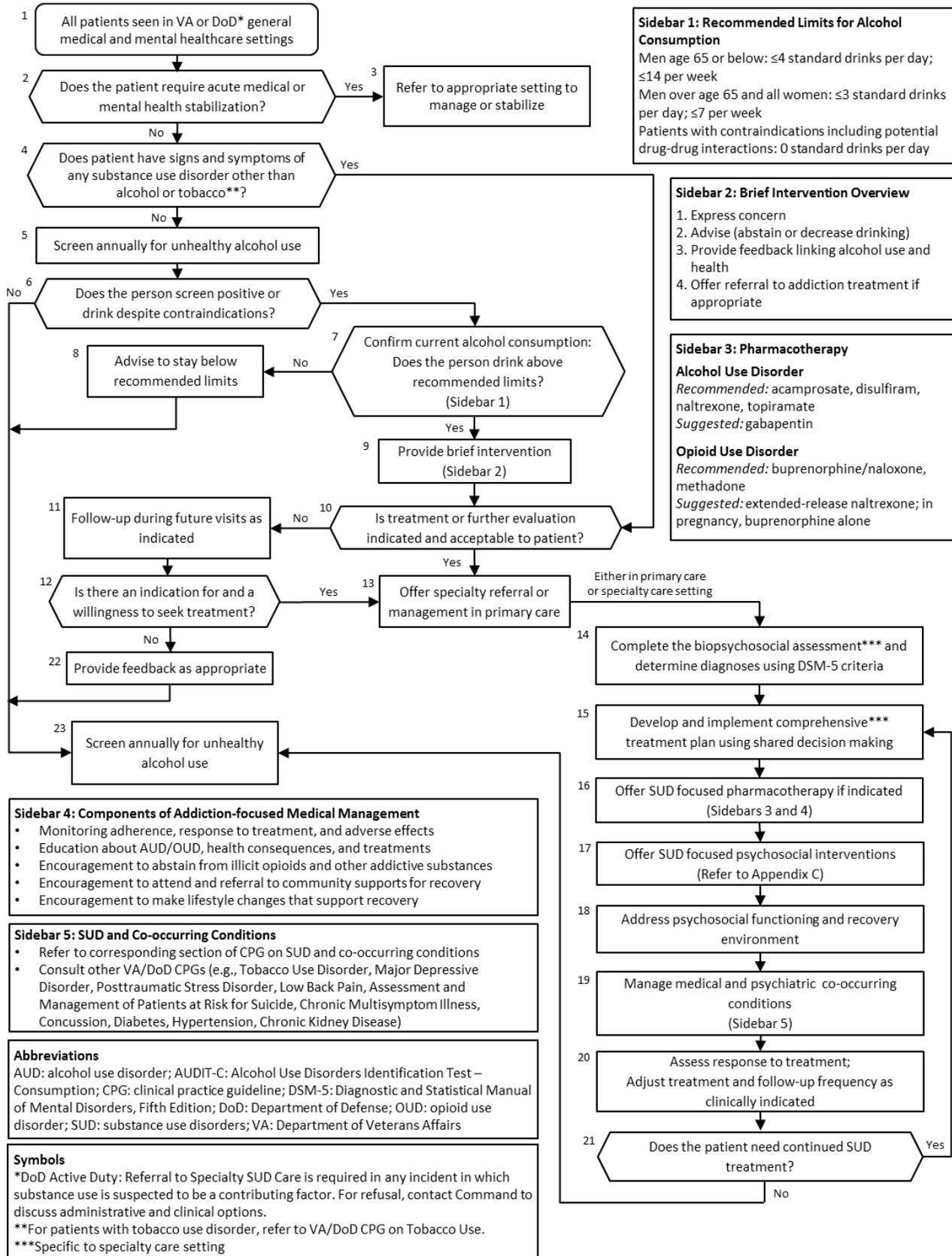
This CPG includes an algorithm which is designed to facilitate understanding of the decision making process used in management of SUD. The use of the algorithm format as a way to represent patient management was chosen based on the understanding that such a format may promote more efficient diagnostic and therapeutic decision making and has the potential to change patterns of resource use. Recognizing that some clinical care processes are non-linear, the algorithm format allows the provider to follow a simplified linear approach in assessing the critical information needed at the major decision points in the clinical process. The algorithm format includes:

- An ordered sequence of steps of care
- Recommended observations and examinations
- Decisions to be considered
- Actions to be taken

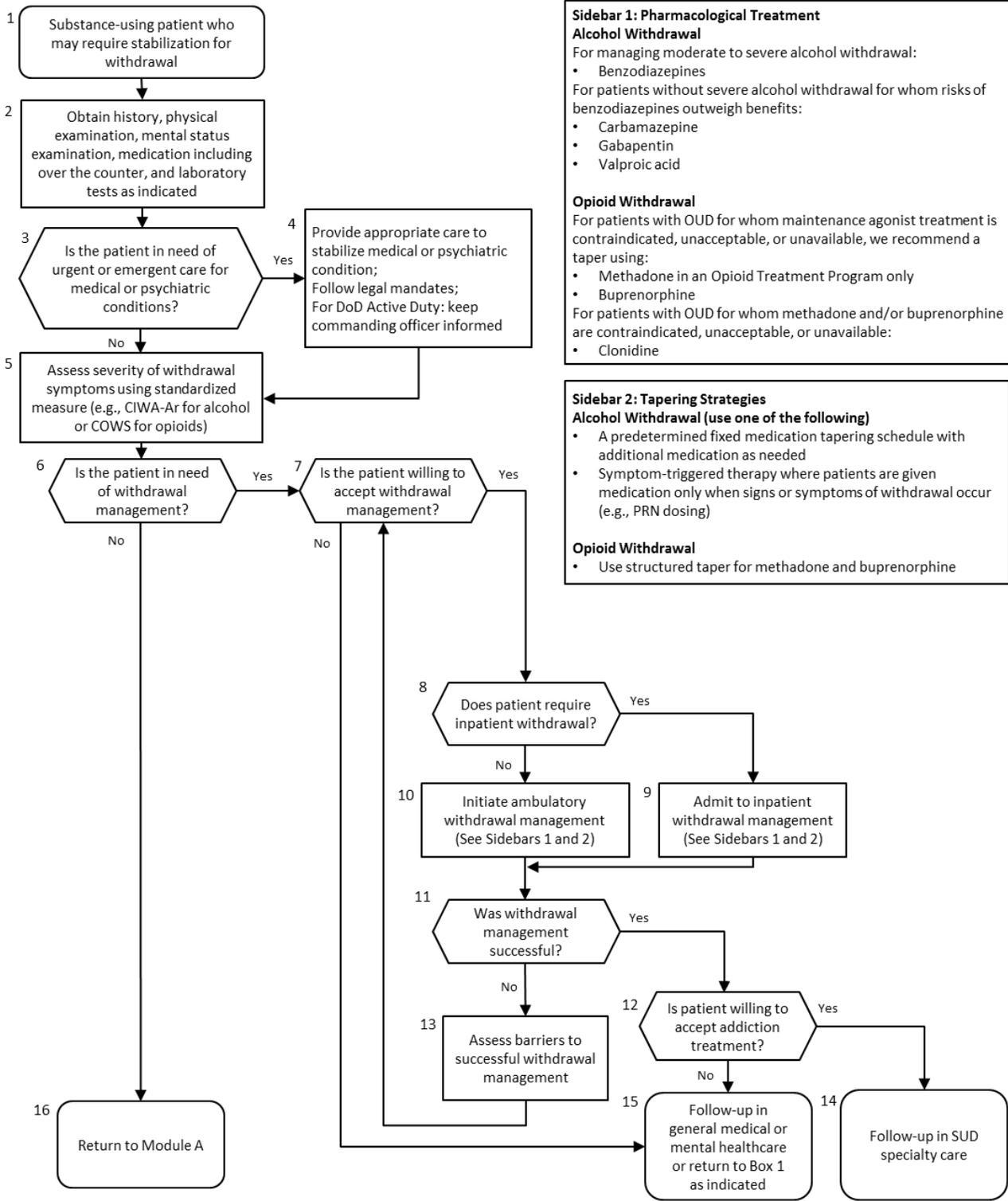
A clinical algorithm diagrams a guideline into a step-by-step decision tree. Standardized symbols are used to display each step in the algorithm, and arrows connect the numbered boxes indicating the order in which the steps should be followed.[\[11\]](#)

	<p>Rounded rectangles represent a clinical state or condition.</p>
	<p>Hexagons represent a decision point in the guideline, formulated as a question that can be answered Yes or No.</p>
	<p>Rectangles represent an action in the process of care.</p>

## A. Module A: Screening and Treatment



## B. Module B: Stabilization



**Sidebar 1: Pharmacological Treatment**

**Alcohol Withdrawal**  
 For managing moderate to severe alcohol withdrawal:  
 • Benzodiazepines  
 For patients without severe alcohol withdrawal for whom risks of benzodiazepines outweigh benefits:  
 • Carbamazepine  
 • Gabapentin  
 • Valproic acid

**Opioid Withdrawal**  
 For patients with OUD for whom maintenance agonist treatment is contraindicated, unacceptable, or unavailable, we recommend a taper using:  
 • Methadone in an Opioid Treatment Program only  
 • Buprenorphine  
 For patients with OUD for whom methadone and/or buprenorphine are contraindicated, unacceptable, or unavailable:  
 • Clonidine

**Sidebar 2: Tapering Strategies**

**Alcohol Withdrawal (use one of the following)**

- A predetermined fixed medication tapering schedule with additional medication as needed
- Symptom-triggered therapy where patients are given medication only when signs or symptoms of withdrawal occur (e.g., PRN dosing)

**Opioid Withdrawal**

- Use structured taper for methadone and buprenorphine

**Abbreviations**  
 AUD: alcohol use disorder; CIWA-Ar: Clinical Institute Withdrawal Assessment for Alcohol-Revised; COWS: Clinical Opiate Withdrawal Scale; DoD: Department of Defense; OUD: opioid use disorder; PRN: as needed

## VIII. Recommendations

#	Recommendation	Strength <sup>1</sup>	Category <sup>1</sup>
<b>A. Screening</b>			
1.	For patients in general medical and mental healthcare settings, we recommend screening for unhealthy alcohol use annually using the three-item Alcohol Use Disorders Identification Test-Consumption (AUDIT-C) or Single Item Alcohol Screening Questionnaire (SASQ).	Strong For	Not reviewed, Amended
<b>B. Brief Alcohol Intervention</b>			
2.	For patients without documented alcohol use disorder who screen positive for unhealthy alcohol use, we recommend providing a single initial brief intervention regarding alcohol-related risks and advice to abstain or drink within nationally established age and gender-specific limits for daily and weekly consumption.	Strong For	Reviewed, New-replaced
<b>C. Determination of Treatment Setting</b>			
3.	For patients with a diagnosis of a substance use disorder, we suggest offering referral for specialty substance use disorder care based on willingness to engage in specialty treatment.	Weak For	Not reviewed, Amended
4.	For patients with substance use disorders, there is insufficient evidence to recommend for or against using a standardized assessment that would determine initial intensity and setting of substance use disorder care rather than the clinical judgment of trained providers.	N/A	Reviewed, New-replaced
<b>D. Treatment</b>			
<b>a. Alcohol Use Disorder</b>			
<i>i. Pharmacotherapy</i>			
5.	For patients with moderate-severe alcohol use disorder, we recommend offering one of the following medications: <ul style="list-style-type: none"> <li>▪ Acamprosate</li> <li>▪ Disulfiram</li> <li>▪ Naltrexone- oral or extended release</li> <li>▪ Topiramate</li> </ul>	Strong For	Reviewed, New-replaced
6.	For patients with moderate-severe alcohol use disorder for whom first-line pharmacotherapy is contraindicated or ineffective, we suggest offering gabapentin.	Weak For	Reviewed, New-replaced
<i>ii. Psychosocial Interventions</i>			
7.	For patients with alcohol use disorder we recommend offering one or more of the following interventions considering patient preference and provider training/competence: <ul style="list-style-type: none"> <li>▪ Behavioral Couples Therapy for alcohol use disorder</li> <li>▪ Cognitive Behavioral Therapy for substance use disorders</li> <li>▪ Community Reinforcement Approach</li> <li>▪ Motivational Enhancement Therapy</li> <li>▪ 12-Step Facilitation</li> </ul>	Strong For	Reviewed, New-replaced

<sup>1</sup> Refer to the full CPG for more information regarding the strength and category of the recommendations.

#	Recommendation	Strength <sup>1</sup>	Category <sup>1</sup>
<b>b. Opioid Use Disorder</b>			
<i>i. Pharmacotherapy</i>			
8.	For patients with opioid use disorder, we recommend offering one of the following medications considering patient preferences: <ul style="list-style-type: none"> <li>■ Buprenorphine/naloxone</li> <li>■ Methadone in an Opioid Treatment Program</li> </ul>	Strong For	Reviewed, New-replaced
9.	In pregnant women with opioid use disorder for whom buprenorphine is selected, we suggest offering buprenorphine alone (i.e., without naloxone) considering patient preferences.	Weak For	Reviewed, New-added
10.	For patients with opioid use disorder for whom buprenorphine is indicated, we recommend individualizing choice of appropriate treatment setting (i.e., Opioid Treatment Program or office-based) considering patient preferences.	Strong For	Reviewed, New-replaced
11.	For patients with opioid use disorder for whom opioid agonist treatment is contraindicated, unacceptable, unavailable, or discontinued and who have established abstinence for a sufficient period of time (see narrative), we recommend offering: <ul style="list-style-type: none"> <li>■ Extended-release injectable naltrexone</li> </ul>	Strong For	Reviewed, New-replaced
12.	There is insufficient evidence to recommend for or against oral naltrexone for treatment of opioid use disorder.	N/A	Reviewed, New-replaced
13.	At initiation of office-based buprenorphine, we recommend addiction-focused Medical Management (see narrative) alone or in conjunction with another psychosocial intervention.	Strong For	Reviewed, New-replaced
<i>ii. Psychosocial Interventions With or Without Pharmacotherapy</i>			
14.	For patients in office-based buprenorphine treatment, there is insufficient evidence to recommend for or against any specific psychosocial interventions in addition to addiction-focused Medical Management. Choice of psychosocial intervention should be made considering patient preferences and provider training/competence.	N/A	Reviewed, New-replaced
15.	In Opioid Treatment Program settings, we suggest offering individual counseling and/or Contingency Management, considering patient preferences and provider training/competence.	Weak For	Reviewed, New-replaced
16.	For patients with opioid use disorder for whom opioid use disorder pharmacotherapy is contraindicated, unacceptable or unavailable, there is insufficient evidence to recommend for or against any specific psychosocial interventions.	N/A	Reviewed, New-replaced
<b>c. Cannabis Use Disorder</b>			
<i>i. Pharmacotherapy</i>			
17.	There is insufficient evidence to recommend for or against the use of pharmacotherapy in the treatment of cannabis use disorder.	N/A	Reviewed, New-added
<i>ii. Psychosocial Interventions</i>			
18.	For patients with cannabis use disorder, we recommend offering one of the following interventions as initial treatment considering patient preference and provider training/competence: <ul style="list-style-type: none"> <li>■ Cognitive Behavioral Therapy</li> <li>■ Motivational Enhancement Therapy</li> <li>■ Combined Cognitive Behavioral Therapy/Motivational Enhancement Therapy</li> </ul>	Strong For	Reviewed, New-replaced

#	Recommendation	Strength <sup>1</sup>	Category <sup>1</sup>
<b>d. Stimulant Use Disorder</b>			
<i>i. Pharmacotherapy</i>			
19.	There is insufficient evidence to recommend for or against the use of any pharmacotherapy for the treatment of cocaine use disorder or methamphetamine use disorder.	N/A	Reviewed, New-added
<i>ii. Psychosocial Interventions</i>			
20.	For patients with stimulant use disorder, we recommend offering one or more of the following interventions as initial treatment considering patient preference and provider training/competence: <ul style="list-style-type: none"> <li>▪ Cognitive Behavioral Therapy</li> <li>▪ Recovery-focused behavioral therapy</li> <li>▪ General Drug Counseling</li> <li>▪ Community Reinforcement Approach</li> <li>▪ Contingency Management in combination with one of the above</li> </ul>	Strong For	Reviewed, New-replaced
<b>E. Promoting Group Mutual Help Involvement</b>			
21.	For patients with substance use disorders in early recovery or following relapse, we recommend promoting active involvement in group mutual help programs using one of the following systematic approaches considering patient preference and provider training/competence: <ul style="list-style-type: none"> <li>▪ Peer linkage</li> <li>▪ Network support</li> <li>▪ 12-Step Facilitation</li> </ul>	Strong For	Reviewed, New-replaced
<b>F. Co-occurring Mental Health Conditions and Psychosocial Problems</b>			
22.	Among patients in early recovery from substance use disorders or following relapse, we suggest prioritizing other needs through shared decision making (e.g., related to other mental health conditions, housing, supportive recovery environment, employment, or related recovery-relevant factors) among identified biopsychosocial problems and arranging services to address them.	Weak For	Not reviewed, Amended
<b>G. Follow-up</b>			
23.	We suggest assessing response to treatment periodically and systematically, using standardized and valid instrument(s) whenever possible. Indicators of treatment response include ongoing substance use, craving, side effects of medication, emerging symptoms, etc.	Weak For	Reviewed, New-replaced
24.	For patients who have initiated an intensive phase of outpatient or residential treatment, we recommend offering and encouraging ongoing systematic relapse prevention efforts or recovery support individualized on the basis of treatment response.	Strong For	Not reviewed, Amended
25.	For patients in substance use disorders specialty care, we recommend against automatic discharge from care for patients who do not respond to treatment or who relapse.	Strong Against	Not reviewed, Amended
<b>H. Stabilization and Withdrawal</b>			
<b>a. Assessment</b>			
26.	For patients with alcohol or opioid use disorder in early abstinence, we suggest using standardized measures to assess the severity of withdrawal symptoms such as Clinical Institute Withdrawal Assessment for Alcohol (revised version) (CIWA-Ar) for alcohol or Clinical Opiate Withdrawal Scale (COWS) for opioids.	Weak For	Not reviewed, Amended

#	Recommendation	Strength <sup>1</sup>	Category <sup>1</sup>
27.	<p>We recommend inpatient medically supervised alcohol withdrawal management for patients with any of the following conditions:</p> <ul style="list-style-type: none"> <li>■ History of delirium tremens or withdrawal seizures</li> <li>■ Inability to tolerate oral medication</li> <li>■ Co-occurring medical conditions that would pose serious risk for ambulatory withdrawal management (e.g., severe coronary artery disease, congestive heart failure, liver cirrhosis)</li> <li>■ Severe alcohol withdrawal (i.e., Clinical Institute Withdrawal Assessment for Alcohol [revised version] [CIWA-Ar] score <math>\geq 20</math>)</li> <li>■ Risk of withdrawal from other substances in addition to alcohol (e.g., sedative hypnotics)</li> </ul>	Strong For	Reviewed, Amended
28.	<p>We suggest inpatient medically supervised withdrawal for patients with symptoms of at least moderate alcohol withdrawal (i.e., Clinical Institute Withdrawal Assessment for Alcohol [revised version] [CIWA-Ar] score <math>\geq 10</math>) and any of the following conditions:</p> <ul style="list-style-type: none"> <li>■ Recurrent unsuccessful attempts at ambulatory withdrawal management</li> <li>■ Reasonable likelihood that the patient will not complete ambulatory withdrawal management (e.g., due to homelessness)</li> <li>■ Active psychosis or severe cognitive impairment</li> <li>■ Medical conditions that could make ambulatory withdrawal management problematic (e.g., pregnancy, nephrotic syndrome, cardiovascular disease, lack of medical support system)</li> </ul>	Weak For	Reviewed, Amended
<b>b. Alcohol Use Disorder Stabilization and Withdrawal</b>			
29.	<p>We recommend using one of the following pharmacotherapy strategies for managing alcohol withdrawal symptoms:</p> <ul style="list-style-type: none"> <li>■ A predetermined fixed medication tapering schedule with additional medication as needed</li> <li>■ Symptom-triggered therapy where patients are given medication only when signs or symptoms of withdrawal occur (e.g., as needed dosing)</li> </ul>	Strong For	Not reviewed, Amended
30.	For treatment of moderate to severe alcohol withdrawal, we recommend using benzodiazepines with adequate monitoring because of documented efficacy and high margin of safety.	Strong For	Reviewed, Amended
31.	For managing mild to moderate alcohol withdrawal in patients for whom risks of benzodiazepines outweigh benefits (e.g., inadequate monitoring available, abuse liability, or allergy/adverse reactions), we suggest considering carbamazepine, gabapentin, or valproic acid as an alternative.	Weak For	Reviewed, New-replaced
32.	We recommend against using alcohol as an agent for medically supervised withdrawal.	Strong Against	Not reviewed, Amended
<b>c. Opioid Use Disorder Stabilization and Withdrawal</b>			
33.	For patients not yet stabilized from opioid use disorder, we recommend against withdrawal management alone due to high risk of relapse and overdose (see Recommendations 8 and 11).	Strong Against	Reviewed, New-replaced

#	Recommendation	Strength <sup>1</sup>	Category <sup>1</sup>
34.	Among patients with opioid use disorder for whom maintenance agonist treatment is contraindicated, unacceptable, or unavailable, we recommend using a methadone (in Opioid Treatment Program only) or buprenorphine taper for opioid withdrawal management (see Recommendation 11).	Strong For	Reviewed, New-replaced
35.	For patients with opioid use disorder for whom methadone and buprenorphine are contraindicated, unacceptable, or unavailable, we recommend offering clonidine as a second-line agent for opioid withdrawal management (see Recommendation 11).	Strong For	Reviewed, New-replaced
<b>d. Sedative Hypnotic Use Disorder Stabilization and Withdrawal</b>			
36.	For patients in need of withdrawal management for sedative hypnotics, we suggest one of the following: <ul style="list-style-type: none"> <li>▪ Gradually taper the original benzodiazepine</li> <li>▪ Substitute a longer acting benzodiazepine then taper gradually</li> <li>▪ Substitute phenobarbital for the addicting agent and taper gradually</li> </ul>	Weak For	Not reviewed, Amended

## IX. Pharmacotherapy for Alcohol Use Disorder and Opioid Use Disorder

**Table 1. Pharmacotherapy for Alcohol Use Disorder**

Naltrexone Oral	Naltrexone Injectable	Acamprosate	Disulfiram	Topiramate <sup>1</sup>	Gabapentin <sup>1</sup>
<b>Indications</b>					
<p>AUD (DSM diagnosis) with:</p> <ol style="list-style-type: none"> <li>At least 3-5 days of pretreatment abstinence not required but may improve response</li> <li>Initial engagement in addiction-focused Medial Management and/or other recommended psychosocial intervention</li> </ol>	<p>AUD (DSM diagnosis) with:</p> <ol style="list-style-type: none"> <li>Pretreatment abstinence not required but may improve response</li> <li>Willingness to receive monthly injections</li> <li>Difficulty adhering to an oral regimen</li> <li>Initial engagement in addiction-focused Medial Management and/or other recommended psychosocial intervention</li> </ol>	<p>AUD (DSM diagnosis) with:</p> <ol style="list-style-type: none"> <li>Abstinence at treatment initiation</li> <li>Initial engagement in addiction-focused Medial Management and/or other recommended psychosocial intervention</li> </ol>	<p>AUD (DSM diagnosis) with:</p> <ol style="list-style-type: none"> <li>Abstinence &gt;12 hours and BAL=0</li> <li>Combined cocaine dependence</li> <li>Previous response to disulfiram</li> <li>Capacity to appreciate risks and benefits and to consent to treatment</li> <li>Initial engagement in addiction-focused Medial Management and/or other recommended psychosocial intervention</li> <li>Note: More effective with monitored administration (e.g., in clinic, with spouse, with probation officer)</li> </ol>	<p>AUD (DSM diagnosis) (off label) with:</p> <ol style="list-style-type: none"> <li>Pretreatment abstinence not required but may improve response</li> <li>Initial engagement in addiction-focused Medial Management and/or other recommended psychosocial intervention</li> </ol>	<p>AUD (DSM diagnosis) (off label) with:</p> <ol style="list-style-type: none"> <li>Pretreatment abstinence not required but may improve response</li> <li>Initial engagement in addiction-focused Medial Management and/or other recommended psychosocial intervention</li> </ol>

<sup>1</sup> Not FDA labeled for treatment of AUD

Naltrexone Oral	Naltrexone Injectable	Acamprosate	Disulfiram	Topiramate <sup>1</sup>	Gabapentin <sup>1</sup>
<b>Contraindications</b>					
<ul style="list-style-type: none"> <li>■ Receiving opioid agonists</li> <li>■ Physiologic opioid dependence with use within past 7 days</li> <li>■ Acute opioid withdrawal</li> <li>■ Failed naloxone challenge test</li> <li>■ Positive urine opioid screen</li> <li>■ Acute hepatitis or liver failure</li> <li>■ Hypersensitivity</li> </ul>	<ul style="list-style-type: none"> <li>■ Receiving opioid agonists</li> <li>■ Physiologic opioid dependence with use within past 7 days</li> <li>■ Acute opioid withdrawal</li> <li>■ Failed naloxone challenge test</li> <li>■ Positive urine opioid screen</li> <li>■ Acute hepatitis or liver failure</li> <li>■ Hypersensitivity</li> <li>■ Inadequate muscle mass</li> </ul>	<ul style="list-style-type: none"> <li>■ Hypersensitivity</li> <li>■ Severe renal insufficiency (CrCl ≤30 mL/min)</li> </ul>	<ul style="list-style-type: none"> <li>■ Severe cardiovascular, respiratory, or renal disease</li> <li>■ Severe hepatic dysfunction (i.e., transaminase levels &gt;3 times upper limit of normal or abnormal bilirubin)</li> <li>■ Severe psychiatric disorders, especially psychotic and cognitive disorders and suicidal ideation</li> <li>■ Poor impulse control</li> <li>■ Metronidazole or ketoconazole therapy which already induce a similar reaction to alcohol</li> <li>■ Hypersensitivity</li> </ul>	<ul style="list-style-type: none"> <li>■ No contraindications in manufacturer's labeling</li> </ul>	<ul style="list-style-type: none"> <li>■ Hypersensitivity</li> </ul>

Naltrexone Oral	Naltrexone Injectable	Acamprosate	Disulfiram	Topiramate <sup>1</sup>	Gabapentin <sup>1</sup>
<b>Warnings/Precautions</b>					
<ul style="list-style-type: none"> <li>Active liver disease</li> <li>Severe renal failure</li> </ul>	<ul style="list-style-type: none"> <li>Active liver disease</li> <li>Uncertain effects (no data) in moderate to severe renal insufficiency</li> <li>Injection site reactions</li> <li>Use intramuscular injections with caution in patients with thrombocytopenia or coagulation disorders</li> </ul>	<ul style="list-style-type: none"> <li>Monitor for emergence of depression or suicidality</li> <li>Reduce dose in patients with renal insufficiency, including elderly</li> </ul>	<ul style="list-style-type: none"> <li>Alcohol-disulfiram reaction; patients must be vigilant to avoid alcohol in all forms including mouthwash, over the counter medications, etc.</li> </ul>	<ul style="list-style-type: none"> <li>Do not abruptly discontinue therapy; taper dosage gradually</li> <li>Cognitive dysfunction, psychiatric disturbances, and sedation may occur with use</li> <li>Increased risk of suicidal ideation with antiepileptic agents, including topiramate</li> </ul>	<ul style="list-style-type: none"> <li>Do not abruptly discontinue therapy; taper dosage gradually</li> <li>May cause CNS depression including somnolence/dizziness</li> <li>Increased risk of suicidal ideation with antiepileptic agents, including gabapentin</li> </ul>
<ul style="list-style-type: none"> <li>Pregnancy Category C</li> </ul>	<ul style="list-style-type: none"> <li>Pregnancy Category C</li> </ul>	<ul style="list-style-type: none"> <li>Pregnancy Category C</li> </ul>	<ul style="list-style-type: none"> <li>Pregnancy Category C</li> </ul>	<ul style="list-style-type: none"> <li>Pregnancy Category C</li> </ul>	<ul style="list-style-type: none"> <li>Pregnancy Category C</li> </ul>
<b>Baseline Evaluation</b>					
<ul style="list-style-type: none"> <li>Liver transaminase levels</li> <li>Bilirubin within normal limits</li> <li>Urine beta-HCG for females</li> </ul>	<ul style="list-style-type: none"> <li>Liver transaminase levels</li> <li>Bilirubin within normal limits</li> <li>CrCl (estimated or measured) 50 mL/min or greater</li> <li>Ensure patient has adequate muscle mass for injection</li> <li>Urine beta-HCG for females</li> </ul>	<ul style="list-style-type: none"> <li>CrCl (estimated or measured)</li> <li>Urine beta-HCG for females</li> </ul>	<ul style="list-style-type: none"> <li>Liver transaminase levels</li> <li>Physical assessment</li> <li>Psychiatric assessment</li> <li>Electrocardiogram if indicated by history of cardiac disease</li> <li>Verify abstinence with breath or BAL</li> <li>Urine beta-HCG for females</li> </ul>	<ul style="list-style-type: none"> <li>Assess renal function</li> <li>Urine beta-HCG for females</li> </ul>	<ul style="list-style-type: none"> <li>Assess renal function</li> <li>Urine beta-HCG for females</li> </ul>

Naltrexone Oral	Naltrexone Injectable	Acamprosate	Disulfiram	Topiramate <sup>1</sup>	Gabapentin <sup>1</sup>
<b>Dosage and Administration</b>					
<ul style="list-style-type: none"> <li>50-100 mg orally 1 time daily</li> </ul>	<ul style="list-style-type: none"> <li>380 mg 1 time monthly by deep intramuscular injection</li> </ul>	<ul style="list-style-type: none"> <li>666 mg orally 3 times daily, preferably with meals</li> </ul>	<ul style="list-style-type: none"> <li>250 mg orally 1 time daily (range, 125-500 mg daily)</li> </ul>	<ul style="list-style-type: none"> <li>Titrate up gradually over several weeks to minimize side effects</li> <li>Initiate at 50 mg/day; increase to a maximum dose of 100 mg 2 times daily</li> </ul>	<ul style="list-style-type: none"> <li>Titrate up gradually to minimize side effects</li> <li>Initiate at 300 mg on day 1 and increase by 300 mg daily as tolerated to target of 1800 mg daily, administered in 3 divided doses</li> </ul>
<b>Alternative Dosing Schedules</b>					
<ul style="list-style-type: none"> <li>25 mg 1- or 2-time(s) daily with meals to reduce nausea, especially during the first week</li> <li>100 mg on Monday and Wednesday and 150 mg on Friday</li> </ul>			<ul style="list-style-type: none"> <li>Reduce dose to 125 mg to reduce side effects</li> <li>For monitored administration, consider giving 500 mg on Monday, Wednesday, and Friday</li> </ul>	<ul style="list-style-type: none"> <li>Geriatric patients with CrCl &lt;70 mL/min/1.73m<sup>2</sup> give initial dose of 25 mg/day followed by incremental increases of 25 mg at weekly intervals until an effective dose is reached</li> </ul>	
<b>Dosing in Special Populations</b>					
<ul style="list-style-type: none"> <li>Hepatic or renal insufficiency: Use caution</li> </ul>	<ul style="list-style-type: none"> <li>Mild renal insufficiency (CrCl 50-80 mL/min): No dosage adjustment necessary</li> <li>Uncertain effects (no data) in moderate to severe renal insufficiency</li> </ul>	<ul style="list-style-type: none"> <li>Moderate renal insufficiency (CrCl 30-50 mL/min): 333 mg 3 times daily</li> <li>Do not administer to patients with severe renal insufficiency (CrCl ≤30 mL/min)</li> </ul>		<ul style="list-style-type: none"> <li>CrCl &lt;70 mL/minute/1.73m<sup>2</sup>: Administer 50% dose and titrate more slowly</li> <li>Dosage adjustment may be required in hepatic impairment</li> </ul>	<ul style="list-style-type: none"> <li>Dosage must be adjusted for renal function, consider target dose &lt;1800 mg daily when CrCl &lt;60 mL/min</li> </ul>

Naltrexone Oral	Naltrexone Injectable	Acamprosate	Disulfiram	Topiramate <sup>1</sup>	Gabapentin <sup>1</sup>
<b>Adverse Effects</b>					
<ul style="list-style-type: none"> <li>Common: Nausea</li> <li>Other: Headache, dizziness, nervousness, fatigue, insomnia, vomiting, anxiety, somnolence</li> </ul>	<ul style="list-style-type: none"> <li>Major: Eosinophilic pneumonia, depression, suicidality</li> <li>Common: Injection-site reactions, injection site tenderness, injection site induration, nausea, headache, asthenia</li> </ul>	<ul style="list-style-type: none"> <li>Major: Suicidality 2.4% (vs. 0.8% on placebo during the first year in clinical trials)</li> <li>Common: Diarrhea (16%)</li> <li>Other: Anxiety, asthenia, depression, insomnia</li> </ul>	<ul style="list-style-type: none"> <li>Major: Hepatotoxicity, peripheral neuropathy, psychosis, delirium, severe disulfiram-ethanol reaction</li> <li>Common: Somnolence, metallic taste, headache</li> </ul>	<ul style="list-style-type: none"> <li>CNS: Paresthesia, nervousness, fatigue, ataxia, drowsiness, lack of concentration, memory impairment, confusion</li> <li>Gastrointestinal: Abdominal pain, anorexia</li> </ul>	<ul style="list-style-type: none"> <li>CNS: Dizziness, drowsiness, ataxia, fatigue</li> <li>Gastrointestinal: Diarrhea, nausea/vomiting, abdominal pain</li> </ul>
<b>Drug Interactions</b>					
<ul style="list-style-type: none"> <li>Opioid-containing medications, including over the counter preparations</li> <li>Thioridazine (increased lethargy and somnolence)</li> </ul>	<ul style="list-style-type: none"> <li>Opioid-containing medications, including over the counter preparations</li> <li>Thioridazine (increased lethargy and somnolence)</li> </ul>	<ul style="list-style-type: none"> <li>Naltrexone: 33% increase in Cmax of acamprosate (no dosage adjustment is recommended)</li> <li>Antidepressants: Weight gain and weight loss more common than with either medication alone</li> </ul>	<ul style="list-style-type: none"> <li>Alcohol containing medications, including over the counter preparations</li> <li>Drug-drug interactions may occur with phenytoin, warfarin, isoniazid, rifampin, diazepam, chlordiazepoxide, imipramine, desipramine, and oral hypoglycemic agents</li> </ul>	<ul style="list-style-type: none"> <li>Use extreme caution if used concurrently with alcohol or other CNS depressants</li> <li>Topiramate may decrease the serum concentrations of contraceptives and decrease their effectiveness</li> </ul>	<ul style="list-style-type: none"> <li>Use extreme caution if used concurrently with alcohol or other CNS depressants</li> <li>Antacids may decrease levels of gabapentin</li> </ul>

Naltrexone Oral	Naltrexone Injectable	Acamprosate	Disulfiram	Topiramate <sup>1</sup>	Gabapentin <sup>1</sup>
<b>Monitoring</b>					
<ul style="list-style-type: none"> <li>■ Repeat liver transaminase levels at 6 and 12 months and then every 12 months thereafter</li> <li>■ Discontinue medication and consider alternatives if no detectable benefit after an adequate trial (50 mg daily for 3 months)</li> </ul>	<ul style="list-style-type: none"> <li>■ Repeat liver transaminase levels at 6 and 12 months and then every 12 months thereafter</li> <li>■ Discontinue if there is no detectable benefit within 3 months</li> </ul>	<ul style="list-style-type: none"> <li>■ Monitor serum creatinine/CrCl, particularly in the elderly and in patients with renal insufficiency</li> <li>■ Maintain therapy if relapse occurs</li> </ul>	<ul style="list-style-type: none"> <li>■ Repeat liver transaminase levels within the first month, then monthly for first 3 months, and periodically thereafter as indicated</li> <li>■ Consider discontinuation in event of relapse or when patient is not available for supervision and counseling</li> </ul>	<ul style="list-style-type: none"> <li>■ Monitor serum creatinine/CrCl periodically, particularly in patients with renal insufficiency and in geriatric patients</li> <li>■ Monitor for change in behavior which might indicate suicidal thoughts or depression</li> <li>■ Discontinue medication and consider alternatives if no detectable benefit after an adequate trial (300 mg daily for 3 months)</li> </ul>	<ul style="list-style-type: none"> <li>■ Monitor serum creatinine/CrCl periodically, particularly in patients with renal insufficiency and in geriatric patients</li> <li>■ Monitor for change in behavior which might indicate suicidal thoughts or depression</li> <li>■ Gabapentin has abuse potential when taken in supratherapeutic dosages; monitor quantities prescribed and usage patterns</li> <li>■ Discontinue medication and consider alternatives if no detectable benefit from at least 900 mg daily for 2-3 months</li> </ul>

Naltrexone Oral	Naltrexone Injectable	Acamprosate	Disulfiram	Topiramate <sup>1</sup>	Gabapentin <sup>1</sup>
<b>Patient Education</b>					
<ul style="list-style-type: none"> <li>Discuss compliance enhancing methods</li> <li>Negotiate commitment from the patient regarding monitored ingestion</li> <li>Side effects, if any, tend to occur early in treatment and can typically resolve within 1-2 weeks after dosage adjustment</li> </ul>	<ul style="list-style-type: none"> <li>Report any concerning injection site reactions</li> <li>Report any new or worsening depression or suicidal thinking</li> <li>May cause allergic pneumonia; contact provider if patient develops signs and symptoms of pneumonia</li> </ul>	<ul style="list-style-type: none"> <li>Report any new or worsening depression or suicidal thinking</li> </ul>	<ul style="list-style-type: none"> <li>Avoid alcohol in food and beverages, including medications</li> <li>Avoid disulfiram if alcohol intoxicated</li> <li>May cause sedation; caution operating vehicles and hazardous machinery</li> <li>Discuss compliance enhancing methods</li> <li>Family members should not administer disulfiram without informing patient</li> <li>Provide patients with wallet cards that indicate the use of disulfiram</li> </ul>	<ul style="list-style-type: none"> <li>Administer without regard to meals</li> <li>It is not recommended to crush, break, or chew immediate release tablets due to bitter taste</li> <li>Caution patients about performing tasks requiring mental alertness</li> </ul>	<ul style="list-style-type: none"> <li>Take first dose on first day at bedtime to minimize somnolence and dizziness</li> <li>Caution patients about performing tasks requiring mental alertness</li> </ul>
<ul style="list-style-type: none"> <li>If signs and symptoms of acute hepatitis occur, discontinue naltrexone and contact provider immediately</li> <li>Very large doses of opioids may overcome the effects of naltrexone and lead to serious injury, coma, or death</li> <li>Small doses of opioids, such as in analgesic, antidiarrheal, or antitussive drugs, may be blocked by naltrexone and fail to produce a therapeutic effect</li> <li>Patients who have previously used opioids may be more sensitive to toxic effects of opioids after discontinuation of naltrexone</li> </ul>					

Abbreviations: AUD: alcohol use disorder; BAL: blood alcohol level; Cmax: maximum concentration; CNS: central nervous system; CrCl: creatinine clearance; DSM: Diagnostic and Statistical Manual of Mental Disorders; HCG: human chorionic gonadotropin; m: meter(s); mg: milligram(s); min: minute(s); mL: milliliter(s)

**Table 2. Pharmacotherapy for Opioid Use Disorder**

Methadone	Buprenorphine/Naloxone or Buprenorphine	Naltrexone Injectable
<b>Indications</b>		
<ul style="list-style-type: none"> <li>■ OUD (DSM diagnosis) and patient meets Federal OTP Standards (42 C.F.R. §8.12)</li> </ul>	<ul style="list-style-type: none"> <li>■ OUD (DSM diagnosis)</li> </ul>	<ul style="list-style-type: none"> <li>■ OUD (DSM diagnosis) with:               <ol style="list-style-type: none"> <li>1. Pretreatment abstinence from opioids and no signs of opioid withdrawal</li> <li>2. Willingness to receive monthly injections</li> </ol> </li> </ul>
<b>Contraindications</b>		
<ul style="list-style-type: none"> <li>■ Hypersensitivity</li> </ul>	<ul style="list-style-type: none"> <li>■ Hypersensitivity</li> </ul>	<ul style="list-style-type: none"> <li>■ Receiving opioid agonists</li> <li>■ Physiologic opioid dependence with use within past 7 days</li> <li>■ Acute opioid withdrawal</li> <li>■ Failed naloxone challenge test</li> <li>■ Positive urine opioid screen</li> <li>■ Acute hepatitis or liver failure</li> <li>■ Hypersensitivity</li> <li>■ Inadequate muscle mass</li> </ul>
<b>Warnings/Precautions</b>		
<ul style="list-style-type: none"> <li>■ Concurrent enrollment in another OTP</li> <li>■ Prolonged QTc interval</li> <li>■ Use caution in patients with respiratory, liver, or renal insufficiency</li> <li>■ Concurrent benzodiazepines or other CNS depressants including active AUD (potential respiratory depression) and other opioid agonists (check PDMP)</li> <li>■ Use of opioid antagonists (e.g., parenteral naloxone, oral or parenteral nalmefene, naltrexone)</li> </ul>	<ul style="list-style-type: none"> <li>■ Buprenorphine/naloxone may precipitate withdrawal in patients on full agonist opioids</li> <li>■ Use caution in patients with respiratory, liver, or renal insufficiency</li> <li>■ Concurrent benzodiazepines or other CNS depressants, including active AUD (potential respiratory depression)</li> <li>■ Use of opioid antagonists (e.g., parenteral naloxone, oral or parenteral nalmefene, naltrexone)</li> </ul>	<ul style="list-style-type: none"> <li>■ Active liver disease</li> <li>■ Uncertain effects (no data) in moderate to severe renal insufficiency</li> <li>■ Injection site reactions</li> <li>■ Use intramuscular injections with caution in patients with thrombocytopenia or coagulation disorders</li> <li>■ Pregnancy Category C</li> </ul>
<b>Baseline Evaluation</b>		
<ul style="list-style-type: none"> <li>■ Consider baseline electrocardiogram and physical examination for patients at risk for QT prolongation or arrhythmias</li> </ul>	<ul style="list-style-type: none"> <li>■ Liver transaminases</li> </ul>	<ul style="list-style-type: none"> <li>■ Liver transaminase levels</li> <li>■ Bilirubin within normal limits</li> <li>■ CrCl (estimated or measured) 50 mL/min or greater</li> <li>■ Ensure patient has adequate muscle mass for injection</li> <li>■ Urine beta-HCG for females</li> </ul>

Methadone	Buprenorphine/Naloxone or Buprenorphine	Naltrexone Injectable
<b>Dosage and Administration</b>		
<ul style="list-style-type: none"> <li>■ Initial dose: 15-20 mg single dose, maximum 30 mg</li> <li>■ Daily dose: Maximum 40 mg/day on first day</li> <li>■ Usual dosage range for optimal effects: 60-120 mg/day</li> <li>■ Titrate carefully, consider methadone's delayed cumulative effects</li> <li>■ Give orally in single dose</li> <li>■ Individualize dosing regimens (avoid same fixed dose for all patients)</li> </ul>	<p>Sublingual dosing:</p> <ul style="list-style-type: none"> <li>■ Induction dose: 2-8 mg 1 time daily</li> <li>■ Day 2 and onward: Increase dose by 2-4 mg/day until withdrawal symptoms and craving are relieved</li> <li>■ Stabilization/maintenance: Titrate by 2-4 mg/day targeting craving and illicit opioid use; usual dose 12-16 mg/day (up to 32 mg/day)</li> <li>■ Individualize dosing regimens</li> <li>■ For any formulation: Do not chew, swallow, or move after placement</li> </ul>	<ul style="list-style-type: none"> <li>■ 380 mg 1 time monthly by deep intramuscular injection</li> </ul>
<b>Alternative Dosing Schedules</b>		
<ul style="list-style-type: none"> <li>■ Give in divided daily doses based on peak and low levels that document rapid metabolism that justifies divided doses</li> </ul>	<ul style="list-style-type: none"> <li>■ Give equivalent weekly maintenance dose divided over extended dosing intervals (2 or 3 times weekly or every 2, 3, or 4 days)</li> </ul>	
<b>Dosing in Special Populations</b>		
<ul style="list-style-type: none"> <li>■ Renal or hepatic impairment: Reduce dose</li> <li>■ Elderly or debilitated: Reduce dose</li> </ul>	<ul style="list-style-type: none"> <li>■ Hepatic impairment: Reduce dose</li> <li>■ For concurrent chronic pain, consider dividing total daily dose into 2- or 3-time daily administration</li> </ul>	<ul style="list-style-type: none"> <li>■ Mild renal insufficiency (CrCl 50-80 mL/min): No dosage adjustment necessary</li> <li>■ Uncertain effects (no data) in moderate to severe renal insufficiency</li> </ul>
<b>Adverse Effects</b>		
<ul style="list-style-type: none"> <li>■ Major: Respiratory depression, shock, cardiac arrest, prolongation of QTc interval on electrocardiogram and torsades de pointes ventricular tachycardia</li> <li>■ Common: Lightheadedness, dizziness, sedation, nausea, vomiting, sweating, constipation, edema</li> <li>■ Less common: Sexual dysfunction</li> </ul>	<ul style="list-style-type: none"> <li>■ Major: Hepatitis, hepatic failure, respiratory depression (usually when misused intravenously or if combined with other CNS depressants)</li> <li>■ Common: Headache, pain, abdominal pain, insomnia, nausea, vomiting, sweating, constipation</li> <li>■ Sublingual buprenorphine/naloxone: Oral hypoesthesia, glossodynia, oral mucosal erythema</li> </ul>	<ul style="list-style-type: none"> <li>■ Major: Eosinophilic pneumonia, depression, suicidality</li> <li>■ Common: Injection site reaction, injection site tenderness, injection site induration, nausea, headache, asthenia</li> </ul>

Methadone	Buprenorphine/Naloxone or Buprenorphine	Naltrexone Injectable
<b>Drug Interactions</b>		
<ul style="list-style-type: none"> <li>■ Drugs that reduce serum methadone levels: Ascorbic acid, barbiturates, carbamazepine, ethanol (chronic use), interferon, phenytoin, rifampin, efavirenz, nevirapine, other antiretrovirals with CYP3A4 activity</li> <li>■ Drugs that increase serum methadone level: Amitriptyline, atazanavir, atazanavir/ritonavir, cimetidine, delavirdine, diazepam, fluconazole, fluvoxamine, ketoconazole, voriconazole</li> <li>■ Opioid antagonists may precipitate withdrawal</li> </ul>	<ul style="list-style-type: none"> <li>■ Drugs that reduce serum buprenorphine level: Ascorbic acid, barbiturates, carbamazepine, ethanol (chronic use), interferon, phenytoin, rifampin, efavirenz, nevirapine, other antiretrovirals with CYP3A4 activity</li> <li>■ Drugs that increase serum buprenorphine level: Amitriptyline, atazanavir, atazanavir/ritonavir, cimetidine, delavirdine, diazepam, fluconazole, fluvoxamine, ketoconazole, voriconazole</li> <li>■ Opioid agonist: Buprenorphine/naloxone or buprenorphine may precipitate withdrawal</li> <li>■ Opioid antagonists may precipitate withdrawal</li> </ul>	<ul style="list-style-type: none"> <li>■ Opioid-containing medications, including over the counter preparations</li> <li>■ Thioridazine (increased lethargy and somnolence)</li> </ul>
<b>Monitoring</b>		
<ul style="list-style-type: none"> <li>■ Signs of respiratory and CNS depression</li> </ul>	<ul style="list-style-type: none"> <li>■ Liver function tests prior to initiation and during therapy</li> </ul>	<ul style="list-style-type: none"> <li>■ Repeat liver transaminase levels at 6 and 12 months and then every 12 months thereafter</li> </ul>

Methadone	Buprenorphine/Naloxone or Buprenorphine	Naltrexone Injectable
<b>Patient Education</b>		
<ul style="list-style-type: none"> <li>■ Strongly advise patient against self-medicating with CNS depressants during methadone therapy</li> <li>■ Serious overdose and death may occur if benzodiazepines, sedatives, tranquilizers, antidepressants, or alcohol are taken with methadone</li> <li>■ Store in a secure place out of the reach of children</li> <li>■ Strongly advise patient to continue in long-term methadone maintenance</li> <li>■ If discontinuing methadone, recommend transition to extended-release injectable naltrexone</li> <li>■ Serious overdose and death may occur if patient relapses to opioid use after withdrawal from methadone</li> </ul>	<ul style="list-style-type: none"> <li>■ Strongly advise patient against self-medicating with CNS depressants during buprenorphine therapy</li> <li>■ Serious overdose and death may occur if benzodiazepines, sedatives, tranquilizers, antidepressants, or alcohol are taken with buprenorphine</li> <li>■ Store in a secure place out of the reach of children</li> <li>■ Strongly advise patient to continue in long-term buprenorphine maintenance</li> <li>■ If discontinuing buprenorphine, recommend transition to extended-release injectable naltrexone</li> <li>■ Serious overdose and death may occur if patient relapses to opioid use after withdrawal from buprenorphine</li> </ul>	<ul style="list-style-type: none"> <li>■ Report any concerning injection site reactions</li> <li>■ Report any new or worsening depression or suicidal thinking</li> <li>■ May cause allergic pneumonia; contact provider if patient develops signs and symptoms of pneumonia</li> <li>■ If signs and symptoms of acute hepatitis occur, discontinue naltrexone and contact provider immediately</li> <li>■ Very large doses of opioids may overcome the effects of naltrexone and lead to serious injury, coma, or death</li> <li>■ Small doses of opioids, such as in analgesic, antidiarrheal, or antitussive drugs, may be blocked by naltrexone and fail to produce a therapeutic effect</li> <li>■ Patients who have previously used opioids may be more sensitive to toxic effects of opioids after discontinuation of naltrexone</li> </ul>

Abbreviations: AUD: alcohol use disorder; CNS: central nervous system; CrCl: creatinine clearance; DSM: Diagnostic and Statistical Manual of Mental Disorders; mg: milligram(s); min: minute(s); mL: milliliter(s); OTP: Opioid Treatment Program; OUD: opioid use disorder; PDMP: prescription drug monitoring program; QTc interval: the heart rate corrected time from the start of the Q wave to the end of the T wave; HCG: human chorionic gonadotropin

**Table 3. Clinical Institute Withdrawal Assessment of Alcohol (CIWA-Ar)**

<b>Patient and Time Information</b>	
Name, date, time, pulse or heart rate taken for one minute, and blood pressure	
<b>Items</b>	
<p><b>Nausea and vomiting:</b> Ask, "Do you feel sick to your stomach? Have you vomited?" Observation.</p> <p>0: No nausea and no vomiting            1: Mild nausea with no vomiting            2            3            4: Intermittent nausea with dry heaves            5            6            7: Constant nausea, frequent dry heaves and vomiting</p>	<p><b>Tactile disturbances:</b> Ask, "Have you had any itching, pins and needles sensations, any burning, any numbness, or do you feel bugs crawling on or under your skin?" Observation.</p> <p>0: None            1: Very mild itching, pins and needles, burning or numbness            2: Mild itching, pins and needles, burning or numbness            3: Moderate itching, pins and needles, burning or numbness            4: Moderately severe hallucinations            5: Severe hallucinations            6: Extremely severe hallucinations            7: Continuous hallucinations</p>
<p><b>Tremor:</b> Arms extended and fingers spread apart. Observation.</p> <p>0: No tremor            1: Not visible, but can be felt fingertip to fingertip            2            3            4: Moderate, with patient's arms extended            5            6            7: Severe, even with arms not extended</p>	<p><b>Auditory disturbances:</b> Ask, "Are you more aware of sounds around you? Are they harsh? Do they frighten you? Are you hearing anything that is disturbing to you? Are you hearing things you know are not there?" Observation.</p> <p>0: Not present            1: Very mild harshness or ability to frighten            2: Mild harshness or ability to frighten            3: Moderate harshness or ability to frighten            4: Moderately severe hallucinations            5: Severe hallucinations            6: Extremely severe hallucinations            7: Continuous hallucinations</p>
<p><b>Paroxysmal sweats:</b> Observation.</p> <p>0: No sweat visible            1: Barely perceptible sweating, palms moist            2            3            4: Beads of sweat obvious on forehead            5            6            7: Drenching sweats</p>	<p><b>Visual disturbances:</b> Ask, "Does the light appear to be too bright? Is its color different? Does it hurt your eyes? Are you seeing anything that is disturbing to you? Are you seeing things you know are not there?" Observation.</p> <p>0: Not present            1: Very mild sensitivity            2: Mild sensitivity            3: Moderate sensitivity            4: Moderately severe hallucinations            5: Severe hallucinations            6: Extremely severe hallucinations            7: Continuous hallucinations</p>

<p><b>Anxiety:</b> Ask, "Do you feel nervous?" Observation.</p> <p>0: No anxiety, at ease</p> <p>1: Mild anxious</p> <p>2</p> <p>3</p> <p>4: Moderately anxious, or guarded, so anxiety is inferred</p> <p>5</p> <p>6</p> <p>7: Equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions</p>	<p><b>Headache, fullness in head:</b> Ask, "Does your head feel different? Does it feel like there is a band around your head?" Do not rate for dizziness or lightheadedness. Otherwise, rate severity.</p> <p>0: Not present</p> <p>1: Very mild</p> <p>2: Mild</p> <p>3: Moderate</p> <p>4: Moderately severe</p> <p>5: Severe</p> <p>6: Very severe</p> <p>7: Extremely severe</p>
<p><b>Agitation:</b> Observation.</p> <p>0: Normal activity</p> <p>1: Somewhat more than normal activity</p> <p>2</p> <p>3</p> <p>4: Moderately fidgety and restless</p> <p>5</p> <p>6</p> <p>7: Paces back and forth during most of the interview, or constantly thrashes about</p>	<p><b>Orientation and clouding of sensorium:</b> Ask, "What day is this? Where are you? Who am I?"</p> <p>0: Oriented and can do serial additions</p> <p>1: Cannot do serial additions or is uncertain about date</p> <p>2: Disoriented for date by no more than 2 calendar days</p> <p>3: Disoriented for date by more than 2 calendar days</p> <p>4: Disoriented for place/or person</p>
<p><b>Scoring</b></p>	
<p>Total CIWA-Ar Score _____</p> <p>Rater's Initials _____</p> <p>Maximum Possible Score: 67</p>	<p>Interpret sum of total scores as follows:</p> <ul style="list-style-type: none"> <li>■ Minimal or absent withdrawal: ≤9</li> <li>■ Mild to moderate withdrawal: 10-19</li> <li>■ Severe withdrawal: &gt;20</li> </ul>

**Table 4. Clinical Opiate Withdrawal Scale (COWS)**

<b>Patient and Time Information</b>	
Name, date, time, reason for this assessment	
<b>Items</b>	
<p><b>Pulse Rate: Record Beats per Minute</b>                      Measured after patient is sitting or lying for one minute                      0: Pulse rate 80 or below                      1: Pulse rate 81-100                      2: Pulse rate 101-120                      4: Pulse rate greater than 120</p>	<p><b>Gastrointestinal Upset: Over Last 1/2 Hour</b>                      0: No gastrointestinal symptoms                      1: Stomach cramps                      2: Nausea or loose stool                      3: Vomiting or diarrhea                      5: Multiple episodes of diarrhea or vomiting</p>
<p><b>Sweating: Over Past 1/2 Hour not Accounted for by Room Temperature or Patient Activity</b>                      0: No report of chills or flushing                      1: Subjective report of chills or flushing                      2: Flushed or observable moistness on face                      3: Beads of sweat on brow or face                      4: Sweat streaming off face</p>	<p><b>Tremor Observation of Outstretched Hands</b>                      0: No tremor                      1: Tremor can be felt, but not observed                      2: Slight tremor observable                      4: Gross tremor or muscle twitching</p>
<p><b>Restlessness Observation During Assessment</b>                      0: Able to sit still                      1: Reports difficulty sitting still, but is able to do so                      3: Frequent shifting or extraneous movements of legs/arms                      5: Unable to sit still for more than a few seconds</p>	<p><b>Yawning Observation During Assessment</b>                      0: No yawning                      1: Yawning once or twice during assessment                      2: Yawning three or more times during assessment                      4: Yawning several times/minute</p>
<p><b>Pupil Size</b>                      0: Pupils pinned or normal size for room light                      1: Pupils possibly larger than normal for room light                      2: Pupils moderately dilated                      5: Pupils so dilated that only the rim of the iris is visible</p>	<p><b>Anxiety or Irritability</b>                      0: None                      1: Patient reports increasing irritability or anxiousness                      2: Patient obviously irritable/anxious                      4: Patient so irritable or anxious that participation in the assessment is difficult</p>
<p><b>Bone or Joint Aches if Patient was Having Pain Previously, only the Additional Component Attributed to Opiate Withdrawal is Scored</b>                      0: Not present                      1: Mild diffuse discomfort                      2: Patient reports severe diffuse aching of joints/muscles                      4: Patient is rubbing joints or muscles and is unable to sit still because of discomfort</p>	<p><b>Gooseflesh Skin</b>                      0: Skin is smooth                      3: Piloerection of skin can be felt or hairs standing up on arms                      5: Prominent piloerection</p>
<p><b>Runny Nose or Tearing Not Accounted for by Cold Symptoms or Allergies</b>                      0: Not present                      1: Nasal stuffiness or unusually moist eyes                      2: Nose running or tearing                      4: Nose constantly running or tears streaming down cheeks</p>	

Scoring	
Total COWS Score _____ Rater's Initials _____ Maximum Possible Score: 48	Interpret sum of total scores as follows: <ul style="list-style-type: none"> <li>■ Mild withdrawal: 5-12</li> <li>■ Moderate withdrawal: 13-24</li> <li>■ Moderately severe withdrawal: 25-36</li> <li>■ Severe withdrawal: &gt;36</li> </ul>

**Table 5. Sedative-hypnotic Conversion [12-17]**

Generic Name	Approximate Equivalents to Diazepam 10 mg or Phenobarbital 30 mg <sup>1</sup>	Time to Peak Plasma level (in Hours)	Half-life Parent Drug (in Hours) <sup>2</sup>	Metabolite Activity (Maximal Half-life in Hours) <sup>3</sup>
Alprazolam	1 mg	1-2	12 ± 2	Inactive
Chlordiazepoxide	25 mg	1-4	10 ± 3.4	Active (up to 120)
Clonazepam	1 mg	1-4	23 ± 5	Inactive
Clorazepate	15 mg	Variable	2 ± 0.9	Active (up to 120)
Diazepam	10 mg	1-2	43 ± 13	Active (up to 120)
Estazolam	1 mg	0.5-0.6	10-24	Inactive
Flurazepam	15 mg	0.5-1.0	74 ± 24	Active (up to 100)
Lorazepam	2 mg	2-4	14 ± 5	Inactive
Oxazepam	30 mg	2-3	8.0 ± 2	Inactive
Quazepam	10 mg	1.5	39	Active (up to 75)
Temazepam	15 mg	2.5	11 ± 6	Inactive
Triazolam	0.25 mg	1-2	2.9 ± 1.0	Inactive
Eszopiclone	15 mg	1	6	Active (<parent)
Zaleplon	20 mg	1	1	Inactive
Zolpidem	20 mg	1.6	2	Inactive
Butalbital	50 mg	1-2	35	Inactive
Pentobarbital	100 mg	0.5-1	15-50	Inactive
Phenobarbital	30 mg	1+	53-140	Inactive
Meprobamate	400 mg	2-3	10	Inactive
Carisoprodol	350 mg	1-3	2	Active (see Meprobamate)
Choral hydrate	250 mg	0.5	<1	Active (up to 94)

Abbreviation: mg: milligrams

<sup>1</sup> Withdrawal doses of diazepam or phenobarbital are those sufficient to suppress most withdrawal symptoms and may not reflect therapeutic dose equivalency.

<sup>2</sup> Half-life of active metabolite(s) may differ.

<sup>3</sup> Primary route of barbiturate elimination is renal excretion.

## XI. Psychosocial Interventions

**Table 6. Summary of Effectiveness of Psychosocial Interventions During Early Recovery (First 90 Days) on Condition Specific Outcomes of Substance Use Disorders (Use or Consequences) or General Psychosocial Functioning**

Interventions (Alphabetical)	First-line Alternatives at Least as Effective as Other Bona Fide Active Interventions or Treatment as Usual				Added Effectiveness as Adjunctive Interventions in Combination with Pharmacotherapy and/or Other First-line Psychosocial Interventions				Comments
	Alcohol	Opioids	Stimulants/ Mixed	Cannabis	Alcohol	Opioids	Stimulants/ Mixed	Cannabis	
<b>Behavioral Couples Therapy (BCT)</b>	√	N/A	N/A	N/A	?	N/A	N/A	N/A	Effective for male or female SUD patients and partners; improves marital satisfaction
<b>Cognitive Behavioral Coping Skills Training</b>	√	N/A	√	√	√	√/?	N/A	√	Added benefit in methadone treatment; Unclear added benefit of CBT in some studies of office-based buprenorphine
<b>Contingency Management (CM)/ Motivational Incentives</b>	N/A	N/A	N/A	N/A	?	√	√	√	CM is recommended only as an adjunctive treatment. CM for cannabis may be problematic given slow clearance in urine
<b>Community Reinforcement Approach (CRA)</b>	√	N/A	√	N/A	N/A	N/A	N/A	N/A	Complex intervention best when including CM
<b>Individual Drug Counseling</b>	N/A	N/A	N/A	N/A	N/A	N/A	√	N/A	One study found benefit when combined with group drug counseling
<b>Motivational Enhancement Therapy (MET)</b>	√	N/A	N/A	√	√	N/A	?	?	Some evidence for those with AUD and low readiness or high anger
<b>12-Step Facilitation (TSF)</b>	√	N/A	N/A	N/A	√	N/A	N/A	N/A	12-step involvement is instrumental in explaining TSF benefits

Symbols: √: Good confidence in effectiveness; ?: Questionable confidence in effectiveness; N/A: Insufficient evidence

Abbreviation: AUD: alcohol use disorder

## XII. Additional Resources

For more information, refer to the full text of the VA/DoD SUD CPG, found at:

<http://www.healthquality.va.gov/guidelines/MH/sud/>. In addition, the following other resources may be helpful:

1. **VA/DoD Clinical Practice Guideline for the Management of Tobacco Use:** Quitting tobacco use has clear benefits in improving ongoing health and decreasing mortality and is strongly encouraged for all patients with SUD. For guidance on the management of tobacco use, please refer to the VA/DoD CPG, available at: <http://www.healthquality.va.gov/guidelines/cd/mtu/>.
2. **Other VA/DoD Clinical Practice Guidelines:** For management of patients presenting with SUD and one of the following conditions, refer to the appropriate VA/DoD CPG, available at <http://www.healthquality.va.gov/>:
  - Bipolar Disorder
  - Chronic Kidney Disease
  - Chronic Multisymptom Illness
  - Diabetes
  - Hypertension
  - Low Back Pain
  - Major Depressive Disorder
  - Mild Traumatic Brain Injury
  - Opioid Therapy for Chronic Pain
  - Posttraumatic Stress Disorder
  - Suicide
3. **Accreditation Standards:** This VA/DoD CPG was developed with a focus on evidence-based practices to help improve patient outcomes. Although they are not explicitly evidence-based, attention should be given to standards provided by various accrediting agencies, most notably, The Joint Commission (TJC) and the Commission on Accreditation of Rehabilitation Facilities (CARF). TJC standards can be found at: [http://www.jointcommission.org/standards\\_information/standards.aspx](http://www.jointcommission.org/standards_information/standards.aspx). CARF standards can be found at: <http://www.carf.org/home/>.

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