San Francisco Department of Public Health
Behavioral Health Services
Medication Use Improvement Committee
1380 Howard St. 5th Floor
San Francisco, CA 94103

Daniel Lurie
Mayor

Medications for Alcohol Use Disorder Guideline

SCOPE: This Medications for Alcohol Use Disorder Guideline is intended to offer prescribing assistance for providers, patients and the interested general public to increase the effectiveness and safety of using medications for Alcohol Use Disorder 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 patient.

INTRODUCTION: Alcohol Use Disorder (AUD) is a common chronic relapsing condition that affects 10.6% of people 12 years and older in the US each year, with an estimated cost of more than $249 billion annually. These costs include the cost to government, costs for binge drinking, underage drinking and drinking while pregnant. However, AUD is greatly undertreated, with only approximately one tenth of those with the disorder receiving treatment each year. Although sustained abstinence may be the ultimate goal, intermittent alcohol use, and even full-blown relapses are to be expected, especially early in treatment. Reductions in alcohol use, and in the harm produced by its ingestion, are extremely important and valuable outcomes.

In 2021, the National Institute on Drug Abuse recommended that the term "medication-assisted treatment" be replaced with references to "pharmacotherapy" or "medications for substance use disorders" when discussing addiction in order to reduce stigma or negative bias. A range of interventions should be considered for all individuals with AUD, including assessment and management of alcohol withdrawal including long-term strategies to support abstinence and reduction in drinking.

ALCOHOL WITHDRAWAL MANAGEMENT: Management of withdrawal from alcohol is a set of focused interventions for managing acute intoxication and withdrawal while the body eliminates alcohol by various metabolic mechanisms. The signs and symptoms of withdrawal generally begin 6 to 24 hours after the last drink or significant reduction in intake. Withdrawal is defined as the development of alcohol-specific behavioral changes, usually with uncomfortable physiological and cognitive consequences resulting from stopping or reducing alcohol intake. Repeated episodes of detoxification and withdrawal are associated with the "kindling" phenomenon, which can lead to more severe and medically complicated subsequent withdrawals and a decrease in seizure threshold. Alcohol withdrawal management, as a brain-protective intervention, should therefore be considered for patients with a long history of heavy drinking. Withdrawal management alone should not be considered as treatment for AUD, but withdrawal management is the first step in the continuum of care and rehabilitation for AUD.

A comprehensive approach to alcohol withdrawal management includes three essential components: *Evaluation, Stabilization,* and *Preparing for continued treatment*.

Evaluation: Includes an assessment of:

- Level of intoxication
- Physiological tolerance
- Past withdrawal management episodes

- History of withdrawal seizures or delirium tremens
- Concurrent use of other central nervous system depressants
- Available social support
- Motivation
- Medical, cognitive and/or psychiatric conditions that may complicate the detoxification episode

The collection of objective data is extremely useful and includes: breathalyzer reading (when possible), vital signs, urine toxicology, and completion of the Clinical Institute Withdrawal Assessment, Revised (CIWA-Ar). The evaluation provides the basis for the initial substance use treatment plan. When determining a patient's level of care, use **Appendix 1** to support decision making. **See Appendix 1 (Alcohol Use Disorder with Physical Dependence and Withdrawal Placement Tree), Appendix 6 (CIWA-Ar), and Appendix 7 (Standard Drink Definitions).**

Stabilization: APatients in alcohol withdrawal should receive pharmacological and psychosocial support from acute intoxication through the completion of successful detoxification. Most patients can successfully navigate withdrawal within 5-7 days. Acutely intoxicated patients may benefit from a coordinated referral to a Sobering Center or another higher level of care, with planned follow-up by the referring provider (see Local Resources). Benzodiazepines represent the standard of care for alcohol withdrawal; however, their use in the ongoing treatment of AUD is unsubstantiated. During alcohol withdrawal management, chlordiazepoxide,lorazepam, or phenobarbital (sometimes used in an ED setting) reduce the risk of seizures, the development of alcohol hallucinosis or delirium tremens and autonomic hyperactivity.

A phenomenon not well documented in the literature, but which has been reported in clinical practice, is protracted withdrawal. Providers should be aware of the symptoms of protracted withdrawal including anxiety, irritability, depressed mood, fatigue, persistent insomnia, impairments in executive functioning, decreased libido and persistent cravings. The symptoms may occur after successful withdrawal management and require clinical attention to ameliorate the high relapse risk at this early stage. **See Appendix 2 (BHS Ambulatory Alcohol Withdrawal Management Protocol).**

Preparing for Continued Treatment: The patient should be actively engaged in some modality of treatment and support in order to seek and maintain stability after completion of detox. This may include treatment of co-occurring psychiatric conditions, addressing protracted withdrawal and attention to destabilizing psychosocial conditions. During this time, the patient is provided with further education about the importance of long-term supports, encouragement, hope, and given appropriate community referrals. For support in developing an appropriate treatment plan for addressing long-term recovery, providers can partner with San Francisco's centralized assessment and referral site for substance use disorders, the Behavioral Health Access Center (BHAC) (see Local Resources). Frequently utilized modalities of care include residential treatment, outpatient treatment, and 12-step programs. In preparation for continued treatment, the provider should discuss and encourage medication options to support long term stability and recovery. **See Appendix 3 for the Pharmacotherapy for Alcohol Use Disorder Table and Appendix 4 for Selection of Pharmacotherapy for Alcohol Use Disorder**.

ALCOHOL USE DISORDER PHARMACOTHERAPY: Three medications- naltrexone, acamprosate, and disulfiram- are approved by the US Food and Drug Administration (FDA) for the treatment of AUD. Each has been shown to reduce cravings to use alcohol, alcohol consumption, and/or relapse into heavy drinking. The agents have different mechanisms of action and vary in appropriateness for different particular patient populations. Of the three, naltrexone has been the best studied in the U.S., and has typically shown the most robust effects. Several additional medications, including gabapentin, topiramate and baclofen have shown some promise, but have yet to be well studied. The latter are not currently FDA-approved medications for AUD. **See Appendix 3 for summary of pharmacotherapy**

options based on recommendations from package inserts and evidence from randomized-controlled trials.

Pharmacotherapy for AUD is ideally started once a patient is abstinent from alcohol as all of the randomized-controlled trials occurred in patients that had been abstinent from alcohol. However, with the exception disulfiram and acamprosate, the agents may be initiated while patients are still using alcohol.

PHARMACOTHERAPY SELECTION: Each medication used for pharmacotherapy of AUD is associated with side effects. Serious complications are rare but may occur. When considering whether to prescribe these medications, the risks must be balanced against the medical, psychiatric, and psychosocial consequences of continued heavy drinking**. See Appendix 4 for decision guidance for selecting a medication based on both published evidence and practical considerations for successful pharmacologic treatment.** In addition, consider the following:

- Patient preference
- Co-morbid conditions
- Patients with a history of response to a particular medication for AUD may be initiated on this agent as first line treatment.

An adequate trial to assess response should be at least 4 weeks. Medication effectiveness is directly related to adherence. Therefore, medication failure cannot be assumed in a patient who is non-adherent to pharmacotherapy. In patients with partial or no response to a medication, consider combination therapy by adding an additional agent or switching to a different agent. While the evidence to support combination therapy is limited, the combination of gabapentin and naltrexone has shown to be more effective than either agent alone.

CO-OCCURING MENTAL ILLNESS: The identification and treatment of underlying psychiatric conditions (e.g., mood disorders, anxiety disorders, and psychotic disorders) with appropriate pharmacotherapy has been shown to indirectly reduce alcohol consumption, in addition to improving overall functioning and quality of life. For additional information, see the SAMHSA Treatment Improvement Protocol (TIP) 42: Substance Abuse Treatment for Persons with Co-Occurring Disorders.

ADOLESCENTS AND YOUNG ADULTS: Adolescence is a unique and critical time for brain development and a vulnerable time for risky behaviors like substance use. The use of substances, like alcohol, has the potential to cause acute and chronic changes and alterations during brain development. Adolescents are more prone than adults to developing dependence symptoms and have difficulty cutting down. The large majority of adolescents with substance use disorder do not access treatment at all for a variety of reasons, including not recognizing the disordered substance use, parents/guardians not being aware, stigma, and lack of treatment availability. Treatment plans for treating AUD in youth should include harm reduction approaches, behavioral therapy referrals, and psychosocial interventions, as well as considering the role of medication for AUD. Case management referrals can be beneficial for connecting youth with providers to help them regularly attend appointments and for supporting both youth and their families as they navigate and link to community resources. Youth should be screened for other co-occurring psychiatric disorders and referred to behavioral services as necessary.

There is currently no FDA-approved medication for the treatment of alcohol use disorder in individuals under the age of 18. Of the three medications FDA-approved for AUD in adults (naltrexone, disulfiram, and acamprosate), only disulfiram and naltrexone have very limited studies among adolescents. Two randomized controlled trials showed preliminary efficacy for the use of disulfiram in lowering relapses, and one randomized controlled trial of oral naltrexone showed minimal efficacy for reducing alcohol consumption. Naltrexone 25-50 mg can be considered in psychosocial treatment-refractory cases in older adolescents and young adults.

OLDER ADULTS: Additional care must be taken to avoid adverse drug effects when using any of the medications commonly used in the younger adult population due to the likelihood of polypharmacy use for co-occurring medical conditions and increased likelihood of impaired hepatic and renal function in the older adult population. A careful review of current medications and of renal and hepatic function, is crucial to ensuring safe medication use, and reduced dosing may be indicated. Disulfiram, in particular, has known adverse interactions with numerous medications.

PREGNANCY/LACTATION*:* Alcohol use during pregnancy has been associated with significnat negative birth outcomes including miscarriage, stillbirth, and premature delivery. It is also associated with significant negative effects for the infant, including fetal alcohol syndrome and fetal alcohol spectrum disorder.

It is important to remember that every pregnancy has at least a 3-5% chance of a birth defect ("background risk"), and the use of any medication during pregnancy should involve an individualized risk-risk-benefit discussion of the risk (to both mother and baby) of untreated or undertreated mental illness, the risk of medication, and the potential benefit of the medication treatment.

. None of the FDA-approved medications for AUD have been adequately studied in human pregnancy or lactation through well-controlled safety trials. Animal studies have shown an increased incidence of early fetal loss and/or teratogenesis when acamprosate and naltrexone were given in high doses to rats and rabbits. A small number of case reports showed fetal malformations in women who had used disulfiram during pregnancy. There is limited data on perinatal safety of topiramate and gabapentin, which are sometimes used as antiepileptics (see Appendix 3). These medications should only be used in pregnant and lactating people when the probable benefits outweigh the risks.

For pregnant patients with AUD, the treating psychiatric clinician should collaborate closely with the Ob-Gyn physician (potentially a Maternal-Fetal Medicine specialist) and seek consultation from a reproductive psychiatrist if indicated.t.

There is inconclusive and inadequate evidence regarding the safety risk of naltrexone, acamprosate, or disulfiram when used during breastfeeding. Naltrexone is known to be excreted into human breast milk.

See the "Safer Prescribing of Sedative-Hypnotics Guideline" for additional information regarding benzodiazepines in pregnancy and lactation.

RENAL AND HEPATIC IMPAIRMENT: See Table 1 below for information on the use of AUD pharmacotherapy in renal and hepatic impairment.

TABLE 1: RENAL AND HEPATIC IMPAIRMENT

Medication	Hepatic Impairment	Renal Impairment
Naltrexone	PO: no data, recommend using long-acting injectable recommendations Long-acting injectable: no adjustment in mild to moderate hepatic impairment (Child-Pugh class A and B). Has not been studied in severe hepatic impairment (Child-Pugh class C)	PO: no data, recommend using long-acting injectable recommendations Long-acting injectable: no adjustment in mild renal impairment (CrCl 50-80 mL/min). Has not been studied in moderate to severe renal impairment (CrCl <50 mL/min)
Disulfiram	Use with caution. Avoid in advanced or severe liver disease. Has been associated	No data. Use with caution due to renal elimination

	with hepatotoxicity and unknown whether there is an increased risk in liver disease.	
Acamprosate	No dose adjustment in mild to moderate hepatic impairment (Child-Pugh A and B). Has not been studied in severe hepatic impairment.	CrCl 30-50 mL/min: reduce initial dose to 333mg TID CrCl <30 mL/min: contraindicated
Baclofen*	No dose adjustment	CrCl 50-80 mL/min: do not exceed 50 mg/day or ~66% of usual maximum dose, whichever is less CrCl 30-<50 mL/min: do not exceed 40 mg/day or ~50% of usual maximum daily dose, whichever is less CrCl <30 mL/min: do not exceed 20 mg/day or ~33% of usual maximum dose, whichever is less
Gabapentin*	No dose adjustment	CrCl 50-79 mL/min: no dose adjustment necessary; usually dosed TID; maximum 1,800 mg/day CrCl 30-49 mL/min: ~50% reduction of total daily dose; dosed BID-TID; max 900 mg/day CrCl 15-29 mL/min: ~75% reduction of total daily dose; dosed daily or BID; max 600 mg/day CrCl <15 mL/min: ~90% reduction of total daily dose; dosed once daily; max 300 mg/day
Topiramate*	Plasma levels increased in hepatic impairment. Use with caution	CrCl <70 mL/min: reduce dose by 1/2

*Off-label use for AUD

RESOURCES IN SAN FRANCISCO:

https://www.sf.gov/information--care-and-treatment-services-addiction-drugs-and-alcohol

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San Francisco Health Network Behavioral Health Services Medication Use Improvement Committee. Safer Prescribing of Psychotropic Medications to Children and Adolescents. 2022. Found at: https://www.sf.gov/resource--2024--medication-guidelines

Pregnancy and Lactation

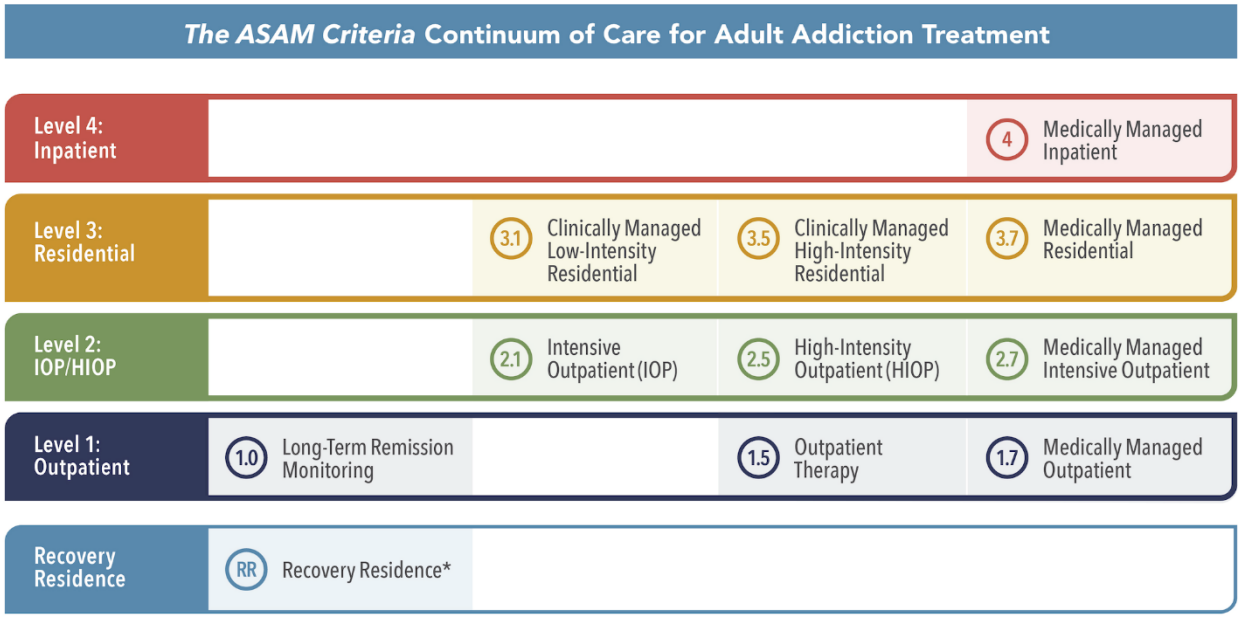
General reference databases: Reprotox, Micromedex, MotherToBaby, LactMed

Massachusetts General Hospital: Center for Women's Mental Health. Psychiatric disorders during pregnancy. Available at: https://womensmentalhealth.org/specialty-clinics/psychiatric-disordersduring-pregnancy/

APPENDIX 1: ALCOHOL USE DISORDER WITH PHYSICAL DEPENDENCE AND WITHDRAWAL PLACEMENT DECISION GUIDANCE

Hospital: ASAM Level 4-WM	Residential Medical Detox: ASAM Level 3.7-WM	Residential Social Detox: ASAM Level 3.2-WM	Outpatient Clinic-Based Detox: ASAM Level 1-WM
• History of seizures or DT's • Delirium, confusion or new onset hallucinations • Moderate to severe tremor and severe anxiety • May concurrently be withdrawing from other substances • Severe destabilizing medical problems present or pose significant risk of consequence during withdrawal • Co-occurring psychiatric disorder is severe • Requires medical monitoring greater than hourly	• History of seizures or DT's possible • Mild to severe tremor, moderate to significant anxiety, and sweating and insomnia • May concurrently be withdrawing from other substances • Moderate to severe active and potentially destabilizing medical problems • Co-occurring psychiatric disorders may be moderate to severe • Low commitment to withdrawal process • Significant risk of relapse	• Low seizure risk • Mild tremor, moderate anxiety, sweating and insomnia • Nausea or vomiting are not greater than moderate • Not withdrawing from other substances • No acute withdrawal in the past year • Co-occurring medical or psychiatric problems are mild or stable • Not stably housed • Inadequate support for ASAM Level 1-WM • Reliability for managing medication impaired • Motivation may be inconsistent/poor • Likelihood of imminent relapse is high	• Low seizure risk • No tremors • Mild anxiety, sweating and insomnia • Not withdrawing from other substances • No acute withdrawal in the past year • Co-occurring medical or psychiatric problems are mild or stable • Housed • Social support – Someone to check in on them in between appointments, e.g., roommate, case manager, family member • Reliable with medication directions • Able to keep medical appointments • Highly motivation

Note the ASAM Criteria Continuum of Care:



APPENDIX 2: AMBULATORY ALCOHOL WITHDRAWAL MANAGEMENT PROTOCOL

The signs and symptoms of alcohol withdrawal generally begin 6 to 24 hours after the last drink or significant reduction in use. Most patients can be detoxified from alcohol in 5-7 days. Ambulatory alcohol withdrawal management should be initiated on a Monday or Tuesday, so that the highest-risk period has passed by the weekend. It is recommended that the patient be seen **daily** for the first three days. The recommendations provided should be tailored to meet the particular circumstances and needs of each patient.

PATIENT SELECTION: If a patient meets any of the following conditions, a higher level of care, including residential or hospital-based detoxification, is indicated:

- A history of delirium tremens, alcohol hallucinosis, or other serious complications related to prior episodes of alcohol withdrawal
- A seizure disorder or alcohol withdrawal seizures within the previous 6 months
- Inability to present sober OR minimal impairment at BAC >0.15 OR daily consumption of >15 standard drinks (See Appendix 6 for Standard Drink Definition)
- Current dependence on benzodiazepines, other sedative-hypnotics (e.g chloral hydrate, carisoprodol, barbiturates), or opioids in addition to alcohol
- Unstable psychiatric or medical conditions that may be exacerbated by withdrawal
- Patients with decompensated liver disease (AST >200, INR >1.5, ascites, esophageal varicies, hepatorenal syndrome, spontaneous bacterial peritonitis, encephalopathy) would be best served in a higher level of care
- Inability to follow instructions (e.g., proper use of medications or adherence with appointments)
- Inability to safely store take-home medication
- Lack of any sober social supports
- Clinical Institute Withdrawal Assessment of Alcohol, revised (CIWA-Ar) score > 18 or any evidence of alcohol hallucinosis, seizure activity, or clouded sensorium (See Appendix 5 for CIWA-Ar)
- Significant vital sign or laboratory abnormalities
- Pregnancy

If a patient meets any of the following, consideration should be given to a higher level of care:

- Recent history of failed ambulatory alcohol withdrawal management
- Concurrent stimulant dependence

EVALUATION:

1. A thorough medical, substance use and psychiatric screening with a focus on history of alcohol withdrawal complications, significant medical or psychiatric conditions, use of other substances of abuse, and current mental status.
2. Labs: check LFTs and INR if concern for impaired liver function. Consider urine toxicology screen and if indicated a pregnancy test.

TREATMENT:

Medication selection: Benzodiazepines are the treatment of choice for alcohol withdrawal. They reduce the risk of seizures, the development of alcohol hallucinosis or delirium tremens, and the autonomic hyperactivity (e.g., tachycardia, hypertension, anxiety) associated with alcohol withdrawal.

- Chlordiazepoxide is recommended for patients without impaired hepatic function (no history of cirrhosis, INR<1.5)
- Lorazepam is recommended for patients with impaired hepatic function

Medication dosing: A combination of a pre-determined gradual taper (based on an initial assessment of risk of withdrawal complications), and the use of the CIWA-Ar scale to evaluate and modify the taper based on symptom presentation should be used. See below for taper dosing schedule.

- Withdrawal complication risk assessment:
    - Low Risk: History of no more than mild withdrawal symptoms, consuming < 10 standard drinks daily, and current CIWA score is < 10
    - Moderate Risk: History of moderate withdrawal symptoms, consuming 10-15 standard drinks daily, or current CIWA score 11-18

Monitoring: If possible, withdrawal should be evaluated daily by the CIWA-Ar Scale.

- If the score is <10, then the taper should be continued as-is.
- If the score is 11-18, then the dose should be increased (by 25-50 mg for chlordiazepoxide OR 0.5-1mg for lorazepam) and/or moving back 1 day in the dosing schedule. May also consider switching from low-risk to moderate-risk schedule.

Typically, patients should receive no more than 24 hours of benzodiazepine at a time to limit risk of overdose and unmonitored withdrawal. “Low-risk” individuals who are particularly motivated, adherent, cognitively intact, healthy, use only alcohol, and may have had successful ambulatory alcohol withdrawal management trials in the past may do well with less frequent monitoring and up to a 72-hour supply of take-home benzodiazepines.

Transfer to higher level of care: If at any point in the withdrawal management process the patient exhibits any evidence of hallucinosis, altered mental status, seizure activity, or a CIWA-Ar score >20, they should be immediately transferred to an emergency room for further care. If the patient continues to drink and/or appears intoxicated, they should also be transferred to a higher level of care.

Supplemental medication: All patients should receive concurrent supplementation with thiamine 100mg PO daily, folate 1mg PO daily, and a daily multivitamin.

Low Risk Dosing Schedule

Days After Alcohol Discontinuation	Adequate Liver Function	Impaired Liver Function/Elderly
1	Chlordiazepoxide 25-50mg po Q6H	Lorazepam 1-2mg po Q6H
2	Chlordiazepoxide 25-50mg po Q6H	Lorazepam 1-2mg po Q6H
3	Chlordiazepoxide 25mg po Q6H	Lorazepam 1mg po Q6H
4	Chlordiazepoxide 25mg po Q8H	Lorazepam 1mg po Q8H
5	Chlordiazepoxide 25mg po Q12H	Lorazepam 0.5-1mg po Q12H

OR

Moderate Risk Dosing Schedule

Days After Alcohol Discontinuation	Adequate Liver Function	Impaired Liver Function/Elderly
1	Chlordiazepoxide 75-100mg po Q6H	Lorazepam 2-3mg po Q6H
2	Chlordiazepoxide 75-100mg po Q6H	Lorazepam 2-3mg po Q6H
3	Chlordiazepoxide 50-75mg po Q6H	Lorazepam 2mg po Q6H
4	Chlordiazepoxide 25-50mg po Q8H	Lorazepam 1-2mg po Q8H
5	Chlordiazepoxide 25mg po Q8H	Lorazepam 0.5-1mg po Q8H
6	Chlordiazepoxide 25mg po Q12H	Lorazepam 0.5mg po Q12H

APPENDIX 3: PHARMACOTHERAPY FOR ALCOHOL USE DISORDER

Medication	Mechanism of Action	Dose & Administration	Contra-indications	Adverse Effects	Comments
Naltrexone PO **Naltrexone long-acting injection (Vivitrol)**	μ opioid antagonist which may block the pleasurable effects of alcohol mediated through the release of endogenous opioids.	Oral: 25mg/day for 3 days then 50mg/day. Can increase to 100mg after 4 weeks if drinking continues. Injection: 380mg IM monthly Recommend patient take with a meal to mitigate nausea Patients must be opioid free for 7-14 days before starting naltrexone, duration of opioid abstinence will depend on half-life of opioids used. Consider naloxone challenge to assess for opioid withdrawal.	Opioid dependence, use, or misuse Decompensated cirrhosis as manifested by AST/ALT > 5x ULN, INR >1.5, ascites, esophageal varices, hepatorenal syndrome, spontaneous bacterial peritonitis, encephalopathy	Nausea, headache, anxiety, sedation. Warnings of hepatotoxic effects are derived from studies using dosages up to 300mg/day for obesity and dementia. No reports of hepatotoxicity at recommended daily dose of 50mg. Insufficient data regarding safety in pregnancy or lactation.	One of the best-studied and underutilized treatments for AUD. Studies favor a reduction in heavy drinking over complete abstinence. ***Monitoring:*** Check LFTs and INR prior to initiation and monitor LFTs periodically while on treatment (annually unless signs or symptoms of hepatitis develop). A pragmatic approach for binge, or high-intensity, drinkers seeking more controlled drinking is the PRN use of naltrexone to reduce craving and decrease the amount of drinking. Naltrexone PRN is a reasonable harm reduction intervention strategy can support and encourage active patient participation in managing the chronic nature ofAUD. The provider directs the patient to take naltrexone 50 mg orally one hour prior to when drinking is expected, such as on weekends, sporting events, holidays or other special events, and that treatment continues indefinitely. This is a generally safe approach for use with patients for whom there are no contraindications for naltrexone.
Disulfiram	Irreversibly inhibits acetald-ehyde dehydro-genase which results in accumula-tion of acetalde-hyde when alcohol is consumed	Begin with 250mg/day, if no effect, consider increasing to 500mg/day Patients must be abstinent from alcohol for $\geq$ 12 hours before initiating therapy.	Underlying coronary artery disease Psychosis Patients unable to abstain or understand severity of alcohol-disulfiram reaction.	Idiosyncratic dose-independent hepatotoxicity, optic neuritis, neuropathies, metallic aftertaste. Rarely may exacerbate psychosis. Insufficient data regarding	An aversive agent intended to dissuade patients from consuming alcohol due to the potential effects of acetaldehyde accumulation. Best data for efficacy under supervised conditions and in open label trials as opposed to blinded trials as participants in blinded trials on placebo may still be dissuaded from drinking out of belief of potential aversive effects.

	producing flushing, tachycar-dia, shortness of breath, headache, and nausea.	Should be dosed in the morning when the desire to abstain from drinking is greatest.	Thiuram derivative allergies	safety in pregnancy or lactation.	Patients need to avoid all exposure to alcohol including sauces, aftershave lotion, mouthwashes, and cough medicines. Effects can last up to 14 days. ***Monitoring:*** Baseline LFTs and after 10-14 days of treatment.
Acamprosate	Modulates hyperactive glutamater-gic NMDA receptors.	666mg TID Creatinine Clearance: 30-50ml/min: 333 mg TID Creatinine Clearance: <30ml/min: contraindicated Following alcohol withdrawal when patient with achieved period of abstinence prior to initiation.	Renal insufficiency with CrCl <30 ml/min	Diarrhea Depression/sui cidality Insufficient data regarding safety in pregnancy or lactation.	High pill burden with TID dosing. Increased rates of relapse if started during detoxification phase, recommend initiation after completed detoxification No reduction in heavy drinking days, but may increase rates abstinence. ***Monitoring:*** Baseline serum creatinine and periodically while on treatment based on clinical assessment
OFF-LABEL					

Baclofen	GABA-B receptor agonist	Initiate 5mg TID and titrate 5mg per dose q3 days up to 10-20mg TID Reduce dose for renal impairments: CrCl: 50-80mL/min: reduce dose by 1/3 CrCl 30-50 mL/min: reduce dose by ½ CrCl <30 mL/min and not on dialysis: reduce dose by 2/3	None. Adjust dose for renal function	Nausea, hypotonia, drowsiness, confusion, Possible dependence	Some data to support increased rates of abstinence compared to placebo. Some evidence that higher doses than those used in trials (60mg vs 30mg/day) may be more effective. ***Monitoring:*** Baseline serum creatinine and periodically while on treatment based on clinical assessment. Insufficient data regarding safety in pregnancy or lactation. Potential for neonatal withdrawal symptoms (increased muscle tone, tremor, jitteriness, seizures) following use during pregnancy. Transmitted into human breast milk.
Gabapentin	Binds to receptors with GABA-like activity modulating release of excitatory neurotrans-mitters.	Titrate up to dose 300-900mg TID, depending on co-occurring conditions (e.g., chronic pain, anxiety) Reduce dose for renal impairments: CrCl 30-59ml/min: ≤700mg BID CrCl 15-29 ml/min: ≤700mg once daily	None. Adjust dose for renal function.	Sedation, dizziness, ataxia, abuse potential. Serious breathing difficulties that can lead to death when used with opioids, other CNS depressants, in those with respiratory impairment or the elderly	Data supporting higher rates of abstinence and lower rates of heavy drinking compared to placebo. ***Monitoring:*** Baseline serum creatinine and periodically while on treatment based on clinical assessment Overall, data does not indicate increased risk of major birth defects or miscarriage, though some studies suggest possible slight increase in congenital malformations risk with first-trimester exposure. Ob-Gyn may recommend folic acid supplementation. Potential for neonatal withdrawal symptoms after concurrent exposure to opioids and gabapentin. Transmitted into human breast milk at low levels. Limited data has not demonstrated safety risk from breast milk exposure.

Topiramate	Attenuates alcohol induced mesolimbic dopamine release by enhancing GABAergic neurotrans-mission at GABA-A receptors and antagonizing glutamatergic neurotrans-mission at non-NMDA receptors	Start at 25mg QHS and titrate by 25mg-50mg increments, up to 150mg BID CrCl < 70 mL/min: dose reduce 50%	None. Adjust dose for renal function. Review potential drug-drug interactions in patients taking additional medications.	Paresthesias, taste perversion, anorexia and weight loss, diarrhea, fatigue and drowsiness, impaired concentration, uncommon but serious metabolic acidosis	Data demonstrates decreased alcohol consumption compared to placebo, shown to be comparable to naltrexone in head to head trials. Side effects common and dose related (recommend gradual titration). Consider as first line therapy in patient with co-occurring seizure disorder ***Monitoring***: Baseline electrolytes and serum creatinine and periodically while on treatment based on clinical assessment Registry data indicates that exposure in first trimester is associated with increased risk of cleft palate and SGA (small for gestational age), and may be associated with preterm delivery or low birth weight. Limited data associates *in utero* exposure with long-term deficits in motor and neurodevelopmental function. Transmitted into human breast milk. Limited reports of infant diarrhea and somnolence after breast milk exposure.

APPENDIX 4: SELECTION OF PHARMACOTHERAPY FOR ALCOHOL USE DISORDER

Level of Recommendation	**Medication**	**Pertinent Treatment Considerations** **(Not exhaustive, see Appendix 3 for details)**
Strongest	Naltrexone	• Most robust effects • Contraindicated in patients taking opioids
Moderate	Topiramate	• Treatment for comorbidities: epilepsy, PTSD hyperarousal symptoms, migraine prophylaxis • Can cause paresthesia (~50% of AUD patients), cognitive slowing (e.g. word-finding) difficulties

		• Relative contraindications (possible fetal risk) in pregnant patient
Moderate	Disulfiram	• Contraindicated in patients unable to remain abstinent from alcohol
	Gabapentin	• Low toxicity risk – safety in overdose • Treatment for comorbidities: insomnia and anxiety during alcohol detox, neuropathic pain
		•
Lowest	Acamprosate	• TID dosing limits utility due to nonadherence • Requires patients be abstinent from alcohol 2 weeks prior to initiation
	Baclofen	• Causes CNS depression, avoid combining with other CNS depressants • Physical dependence

APPENDIX 5: CLINICAL INSTITUTE WITHDRAWAL ASSESSMENT OF ALCOHOL SCALE, REVISED (CIWA-AR)

Patient:_____ Date: _____ Time: _____

Pulse or heart rate, taken for one minute:_____ Blood pressure:_____

NAUSEA AND VOMITING -- *Ask "Do you feel sick to your stomach? Have you vomited?" Observation.* 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	**TACTILE DISTURBANCES** -- *Ask "Have you any itching, pins and needles sensations, any burning, any numbness, or do you feel bugs crawling on or under your skin?" Observation.* 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
TREMOR -- *Arms extended and fingers spread apart. Observation.* 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	**AUDITORY DISTURBANCES** -- *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.* 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
PAROXYSMAL SWEATS -- *Observation.* 0 no sweat visible 1 barely perceptible sweating, palms moist 2 3 4 beads of sweat obvious on forehead 5 6 7 drenching sweats	**VISUAL DISTURBANCES** -- *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.* 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
ANXIETY -- *Ask "Do you feel nervous?" Observation.*	**HEADACHE, FULLNESS IN HEAD** -- *Ask "Does your head feel different? Does it feel like there is a band*

0 no anxiety, at ease 1 mild anxious 2 3 4 moderately anxious, or guarded, so anxiety is inferred 5 6 7 equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions	*around your head?" Do not rate for dizziness or lightheadedness. Otherwise, rate severity.* 0 not present 1 very mild 2 mild 3 moderate 4 moderately severe 5 severe 6 very severe 7 extremely severe
AGITATION -- *Observation.* 0 normal activity 1 somewhat more than normal activity 2 3 4 moderately fidgety and restless 5 6 7 paces back and forth during most of the interview, or constantly thrashes about	**ORIENTATION AND CLOUDING OF SENSORIUM** *– Ask "What day is this? Where are you? Who am I?"* 0 oriented and can do serial additions 1 cannot do serial additions or is uncertain about date 2 disoriented for date by no more than 2 calendar days 3 disoriented for date by more than 2 calendar days 4 disoriented for place/or person

Total **CIWA-Ar** Score _____
Rater's Initials _____
Maximum Possible Score 67

*The **CIWA-Ar** is not* copyrighted and may be reproduced freely. This assessment for monitoring withdrawal symptoms requires approximately 5 minutes to administer. The maximum score is 67 (see instrument). Patients scoring less than 10 do not usually need additional medication for withdrawal.

Sullivan, J.T.; Sykora, K.; Schneiderman, J.; Naranjo, C.A.; and Sellers, E.M. Assessment of alcohol withdrawal: The revised Clinical Institute Withdrawal Assessment for Alcohol scale (**CIWA-Ar**). *British Journal of Addiction* 84:1353-1357, 1989.**Training Video**
For education about scoring a CIWA-Ar, see below video:
https://www.youtube.com/watch?v=NUKigZjcGy4

APPENDIX 6: STANDARD DRINK DEFINITION

	Standard Drink Equivalents	Approximate Number of Standard Drinks In:
Beer or Cooler (~5% alcohol)	12 oz.	12 oz. = 1 16 oz. = 1.3 22 oz. = 2 40 oz. =3.3
Malt Liquor (~7% alcohol)	8-9 oz.	12 oz. = 1.5 16 oz. = 2 22 oz. = 2.5 40 oz. = 4.5
Table Wine (~12% alcohol)	5 oz.	750 mL (25 oz.) bottle = 5
80-proof Distilled Spirits (40% alcohol)	1.5 oz.	mixed drink = 1 or more pint (16 oz.) = 11 fifth (25 oz.) = 17 1.75 L (59 oz.) = 39

Note: Many contemporary beers and wines have higher ABV than those listed above, so actual alcohol intake may be higher than suggested here,

Reference

National Institute on Alcohol Abuse and Alcoholism. A Pocket Guide for Alcohol Screening and Brief Intervention. 2005 Ed. Found at:
http://pubs.niaaa.nih.gov/publications/Practitioner/PocketGuide/pocket.pdf