CLINICAL GUIDELINES PROGRAM
NEW YORK STATE DEPARTMENT OF HEALTH AIDS INSTITUTE | HIV · HCV · SUBSTANCE USE · LGBT HEALTH

Treatment of Alcohol Use Disorder

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Purpose and Development of This Guideline

This guideline on the treatment of alcohol use disorder (AUD) was developed by the New York State Department of Health AIDS Institute (NYSDOH AI) to guide primary care providers and other practitioners in New York State in treating individuals with AUD.

This guideline aims to:

- Increase the number of clinicians in outpatient settings offering evidence-based treatment to individuals with AUD.
- Increase the number of New York State residents with AUD who are engaged in treatment.
- Reduce the number of alcohol-related deaths in New York State.
- Promote a harm reduction approach to treatment of AUD, which involves practical strategies and ideas aimed at reducing the negative consequences associated with alcohol use.
  - See the NYSDOH AI guideline *Harm Reduction Approach to Treatment of All Substance Use Disorders*.

Alcohol Use Disorder in the United States

In the 2018 National Survey on Drug Use and Health in the United States, the Substance Use and Mental Health Services Administration (SAMHSA) reported that an estimated 14.8 million individuals aged 12 or older in the United States had AUD, based on *Diagnostic and Statistical Manual of Mental Disorders-IV* criteria [SAMHSA 2019]. SAMHSA also reported that approximately:

- 67.1 million individuals engaged in binge drinking on at least 1 day within the past 30 days, defined as 5 or more drinks at 1 occasion for men and 4 or more for women.
- 16.6 million individuals aged 12 or older engaged in heavy drinking within the past 30 days, defined as binge drinking on 5 or more days [SAMHSA 2019].

The most recent available analysis of alcohol-related mortality in the United States was based on death certificates and indicated that, among individuals aged 16 years and older, death rates due to alcohol increased by 50.9% between 1999 and 2017. In 2017, 2.6% of approximately 2.8 million deaths in the United States involved alcohol, with liver disease and alcohol overdose or overdose with alcohol and other drugs accounting for nearly half of alcohol-related deaths [White, et al. 2020].

Role of Primary Care Providers in the Treatment of Alcohol Use Disorder

Primary care providers in NYS can play an essential role in identifying and treating AUD in their patients. There are effective pharmacologic and psychosocial treatments for AUD that can be delivered in an outpatient setting, which can increase access to evidence-based treatment for individuals with AUD. Because primary care may lend itself to long-term, continuous relationships, this treatment setting lends itself well to managing AUD, a chronic health condition, because it allows for ongoing follow-up.

Development of This Guideline

This guideline was developed by the NYSDOH AI Clinical Guidelines Program, which is a collaborative effort of the NYSDOH AI Office of the Medical Director and the Johns Hopkins University School of Medicine, Division of Infectious Diseases.

Established in 1986, the goal of the Clinical Guidelines Program is to develop and disseminate evidence-based, state-of-the-art clinical practice guidelines to improve the quality of care throughout New York State for people who have HIV,

hepatitis C virus, or sexually transmitted infections; people with substance use issues; and members of the LGBTQ community. NYSDOH AI guidelines are developed by committees of clinical experts through a consensus-driven process.

The NYSDOH AI charged the Substance Use Guidelines Committee with developing evidence-based clinical recommendations to guide primary care and other medical care providers in treating individuals with AUD. The resulting recommendations are based on extensive review of the medical literature and reflect consensus among the committee members. Each recommendation is rated for strength and quality of the evidence based on the rating scheme below. If a recommendation is based on expert opinion, the rationale for the opinion is provided in the text.

AIDS Institute Clinical Guidelines Program Recommendations Rating Scheme	
Strength of Recommendation	**Quality of Supporting Evidence**
A = Strong	1 = At least 1 randomized trial with clinical outcomes and/or validated laboratory endpoints
B = Moderate	2 = One or more well-designed, nonrandomized trial or observational cohort study with long-term clinical outcomes
C = Optional	3 = Expert opinion

Goals of Treatment for Alcohol Use Disorder and Treatment Options

☑ RECOMMENDATIONS

Treatment Options

- Clinicians should inform patients with alcohol use disorder (AUD) about all available pharmacologic and psychologically based treatment options and all available treatment settings, including outpatient primary care and addiction specialty treatment (intensive outpatient, inpatient, and residential treatments). (A3)

Choosing a Treatment Option

- Clinicians should recommend pharmacologic treatment for individuals with moderate-to-severe AUD (see *Table 1: Pharmacologic Treatment of Alcohol Use Disorder in Nonpregnant Adults*). (A1)
  - Clinicians should recommend oral acamprosate or oral or injectable extended-release (XR) naltrexone as the preferred medications for treating AUD. (A1)
- Clinicians and patients should choose a pharmacologic agent based on: (A3)
  - Evidence-based recommendations.
  - Ease of administration.
  - Available formulations.
  - Adverse effects.
  - Presence of medical conditions (e.g., hepatic or renal disease, conditions that require treatment with opioids).
  - Comorbid psychiatric conditions (e.g., depression, anxiety) and/or substance use disorders (e.g., opioid use disorder, tobacco use disorder).
  - Presence of specific features of AUD (e.g., craving).
  - Patient preference.
- Clinicians should recommend psychologically based treatment for individuals with AUD. (A1)

Goals of Treatment

A traditional goal of treatment for alcohol use disorder (AUD) is long-term cessation of alcohol use. Because this goal may not be achievable for many individuals, alternative goals can lead to substantial improvements in the health and lives of those with AUD. Such alternatives may include:

- Staying engaged in care, which can also facilitate prevention, diagnosis, and treatment of other conditions.
- Reducing alcohol use.
- Reducing high-risk behaviors (e.g., driving while intoxicated, alcohol-related unprotected sex).
- Improving quality of life and other social indicators, such as employment, stable housing, and risk of incarceration.
- Improving mental health.

As with other chronic conditions, treatment goals for AUD should be individualized and are likely to change over time. It is important for healthcare providers and patients to discuss, agree on, and review AUD treatment goals regularly. If patients are unable to meet treatment goals, intensifying treatment with frequent visits, behavioral interventions, mental health assessment and treatment, and adjustment of dose or type of medication may be warranted.

Pharmacologic Treatment Options

Currently, 3 medications are approved by the U.S. Food and Drug Administration (FDA) for the treatment of AUD: acamprosate, naltrexone, and disulfiram. Gabapentin and topiramate are additional evidence-based options for treatment. All of these medications are available in oral formulations, and naltrexone is also available in an extended-release (XR) formulation for intramuscular injection.

Based on strong clinical evidence, acamprosate and oral or XR naltrexone are the preferred pharmacologic treatments for individuals with moderate-to-severe AUD who have a goal of reducing or abstaining from alcohol use [Jonas, et al. 2014; SAMHSA 2015]. In individuals with mild AUD, clinicians may consider pharmacologic treatment with oral acamprosate or oral or XR naltrexone.

Clinical trials directly comparing acamprosate and naltrexone have not consistently established the superiority of one medication over the other in reducing heavy drinking. Individuals who use alcohol primarily for positive reinforcement (reward drinkers) may benefit more from naltrexone than those who drink for negative reinforcement, such as avoiding withdrawal (relief drinkers) [Mann, et al. 2018]. There is minimal and mixed evidence on whether combining naltrexone and acamprosate has an additive effect on alcohol consumption outcomes [Kiefer, et al. 2003; Anton, et al. 2006].

Acamprosate: Alcohol withdrawal produces a neurobiologic derangement in neuronal gamma-aminobutyric acid type A ($GABA_A$), *N*-methyl-*D*-aspartic acid (NMDA), and glutamate transmission, which can result in an excitotoxic state and neuronal injury. Acamprosate modulates transmissions from $GABA_A$ and NMDA receptors, which can restore neuronal balance and mitigate the associated symptoms [Kalk and Lingford-Hughes 2014].

In clinical trials that have compared treatment with acamprosate and placebo, acamprosate increased the proportion of individuals who maintained complete abstinence from alcohol (complete abstinence rate), the mean cumulative abstinence duration, the percentage of alcohol-free days, and the median time to first drink [Paille, et al. 1995; Sass, et al. 1996; Whitworth, et al. 1996; Geerlings, et al. 1997; Pelc, et al. 1997; Poldrugo 1997; Tempesta, et al. 2000; Gual and Lehert 2001; Higuchi 2015; Plosker 2015]. A meta-analysis from 2014 found that acamprosate was significantly associated with decreased return to any drinking and with decreased percentage of drinking days throughout treatment [Jonas, et al. 2014]. Acamprosate should be initiated as soon as the individual has abstained from alcohol use (within 7 days) for the best treatment response. Acamprosate can be initiated if the individual is still actively using alcohol, but the efficacy of treatment during active alcohol use is unknown.

Naltrexone: Naltrexone is an opioid receptor antagonist used in the treatment of individuals with AUD or opioid use disorder (OUD). Alcohol use increases the activity of the endogenous opioid system. As an opioid receptor antagonist, naltrexone interferes with the rewarding aspects of alcohol [Mason, et al. 2002; Pettinati, et al. 2006; Ray, et al. 2010]. Naltrexone may also decrease subjective cravings for alcohol [Maisel, et al. 2013]. A meta-analysis found no significant difference in alcohol consumption, a measure combining study-specific outcomes, between naltrexone and acamprosate treatment [Kiefer, et al. 2003; Anton, et al. 2006; Morley, et al. 2006; Mann, et al. 2013; Jonas, et al. 2014].

Clinical trials have shown that naltrexone improves alcohol use outcomes and, specifically, decreases the likelihood of return to drinking and the overall number of drinking days [Jonas, et al. 2014]. A meta-analysis of studies evaluating treatment with oral naltrexone showed that oral naltrexone 50 mg daily was associated with decreased return to any drinking and decreased return to heavy drinking, and XR naltrexone was associated with reduced heavy drinking days [Jonas, et al. 2014]. An ongoing randomized controlled trial by Lee, et al., is examining the effectiveness of oral versus XR naltrexone in producing abstinence or moderate drinking [Malone, et al. 2019]. Studies have shown that naltrexone is more effective in reducing alcohol consumption in individuals who use nicotine or cigarettes compared with those who do not [Fucito, et al. 2012; Anton, et al. 2018], which may be one factor in selecting pharmacologic treatment. Active alcohol

use is not a contraindication to initiating treatment with naltrexone (oral and XR formulations); however, individuals should be monitored for alcohol withdrawal syndrome if alcohol use is significantly reduced abruptly.

Disulfiram: Disulfiram inhibits the enzyme aldehyde dehydrogenase, which breaks down acetaldehyde, an alcohol byproduct. Consuming alcohol while taking disulfiram results in an accumulation of acetaldehyde and adverse reactions such as low blood pressure, tachycardia, facial flushing, nausea, vomiting, dyspnea, sweating, dizziness, blurred vision, and confusion. This adverse reaction is called the disulfiram-ethanol reaction [Bell and Smith 1949]. The psychological threat of these unpleasant physiologic effects is believed to be the primary mechanism for dissuading alcohol use in individuals with AUD [Skinner, et al. 2014].

Evidence is mixed on the effectiveness of disulfiram for the treatment of AUD. Well-controlled clinical trials do not support an association between disulfiram use and improvement in alcohol consumption outcomes [Jonas, et al. 2014]. However, it may be difficult to evaluate disulfiram in a double-blind study design because the threat of the physiologic effects of combining alcohol and disulfiram, which is present for both treatment and control groups, is directly related to the efficacy of the drug [Skinner, et al. 2014]. A meta-analysis showed that disulfiram was effective at improving consumption outcomes in open-label trials (no blinding for participants or researchers) but not effective in blinded randomized controlled trials [Skinner, et al. 2014].

Since the 1970s, studies examining the effectiveness of disulfiram have typically compared unsupervised administration of disulfiram with administration supervised by health professionals or by suitable delegated associates of the participant. Results suggest that disulfiram can be an effective treatment with supervised administration, but adherence is low with unsupervised administration [Fuller, et al. 1986; Jorgensen, et al. 2011; Skinner, et al. 2014; Brewer, et al. 2017]. Active alcohol use is a contraindication to disulfiram. At least 12 hours of abstinence from alcohol is required before initiating treatment with disulfiram to avoid an adverse reaction. Individuals should be warned that reactions may occur if alcohol is consumed up to 14 days after taking disulfiram.

Gabapentin: The mechanism of action of gabapentin in treating AUD is not fully understood. However, evidence suggests that gabapentin modulates and stabilizes central stress systems that are dysregulated by the cessation of alcohol use [Roberto, et al. 2008; Roberto, et al. 2010].

Although gabapentin is not approved by the FDA for treatment of AUD, use of this medication has been associated with reductions in alcohol use and craving [Mason, et al. 2014; Mason, et al. 2018]. In addition, as an adjunct to benzodiazepines, gabapentin is effective in treating common symptoms of acute and protracted alcohol withdrawal, including anxiety and sleep disturbances [Karam-Hage and Brower 2000; Bazil, et al. 2005; Brower, et al. 2008; Myrick, et al. 2009; Lavigne, et al. 2012; Rosenberg, et al. 2014; Mason, et al. 2018]. Active alcohol use is not a contraindication to initiating gabapentin [Myrick, et al. 2007].

Topiramate: The mechanism of action of topiramate in treating AUD is not fully understood. However, evidence suggests that topiramate enhances GABAergic neurotransmission and suppresses glutamatergic neurotransmission, helping to normalize and restore balance in the reward circuits of the brain [Shank and Maryanoff 2008; Frye, et al. 2016; Cheng, et al. 2018].

Like gabapentin, topiramate is not approved by the FDA for treatment of AUD, but it has been associated with fewer drinking days, fewer drinks per drinking day, decreased percentage of heavy drinking days, and increased number of abstinent days [Manhapra, et al. 2019]. To a lesser degree, topiramate has been associated with reduced cravings for alcohol [Manhapra, et al. 2019].

The effectiveness of topiramate for AUD does not appear to be substantially affected by whether or not the individual was abstinent from alcohol or underwent detoxification from alcohol before treatment. This suggests that topiramate can be used successfully in individuals who are unwilling or unable to achieve abstinence before treatment [Maisel, et al. 2013].

***Diagnostic and Statistical Manual of Mental Disorders-IV* (*DSM-IV*) and *DSM-5* Diagnoses**
• In most published studies of pharmacologic treatment for alcohol use, participants had a *DSM-IV* diagnosis of "alcohol dependence," which approximately corresponds to "moderate-to-severe AUD" in the *DSM-5* [Compton, et al. 2013; Hasin, et al. 2013; Peer, et al. 2013]. Thus, recommendations for pharmacologic treatment in this guideline are made for patients who meet *DSM-5* criteria for moderate-to-severe AUD. • In most published studies of psychosocial treatment for alcohol use, participants had a *DSM-IV* diagnosis of "alcohol abuse" or "alcohol dependence." Alcohol abuse approximately corresponds to "mild AUD" in the *DSM-5*. Thus, recommendations for psychosocial treatment in this guideline are made for patients who meet the current *DSM-5* criteria for mild, moderate, or severe AUD.

Non-Pharmacologic Treatment

Psychologically based treatment: In general, psychologically based treatment for AUD is delivered in a specialty addiction treatment program. In addition to offering patients pharmacologic treatment, clinicians should refer patients for psychological interventions, based on individual needs, social factors, preferences, and resources.

Many studies support the effectiveness of motivational interviewing (MI), motivational enhancement therapy (MET), and cognitive behavioral therapy (CBT) for treating individuals with AUD [Magill and Ray 2009; Lundahl BW, et al. 2010; Smedslund, et al. 2011; Lundahl B, et al. 2013; Lenz, et al. 2016; DiClemente, et al. 2017; ASAM 2019], including studies conducted in the primary care setting [Stecker, et al. 2012; Lundahl B, et al. 2013; VanBuskirk and Wetherell 2014]. Evidence is mixed about whether the combination of pharmacologic treatment with a structured psychosocial intervention leads to better outcomes than pharmacologic treatment alone for individuals with AUD [Anton, et al. 2006].

MI, MET, CBT, and other approaches have been incorporated into many interventions for treatment of AUD. Variables in studies of psychologically based interventions for alcohol use make it difficult to compare and interpret the evidence and extrapolate it to "real-world" settings and individual patients. These variables include type of approach, duration and number of sessions, type and training of the healthcare provider delivering the intervention, treatment setting, mode of delivery (in person or computerized), individual or group setting, risk level of alcohol use or AUD, and concurrent pharmacologic treatment. Most clinical trials examining pharmacologic treatment include a psychological component (e.g., MI or CBT for all treatment groups).

MI is a way of helping patients recognize their current or potential problems and take action toward resolving them. The overall goal of MI is to increase the patient's intrinsic motivation to facilitate change from within, and the method is particularly useful for patients who are ambivalent about changing behavior or who are reluctant to change [Miller 2002]. This technique emphasizes the autonomy of the patient while providing a safe space for collaboration and consistent engagement to enhance the patient's motivation for change. The MI approach also helps the clinician identify the patient's readiness to change behavior and to use the patient's level of readiness as a starting point for counseling or treatment. It is worthwhile for healthcare providers to understand and use an MI-style approach when discussing alcohol use and AUD treatment plans with patients and to be aware of clinician and patient resources (see *Online Resources: Psychologically Based Treatment for AUD*, below).

The key principles of MI are:

- Express empathy/avoid arguing.
- Develop discrepancy.
- Roll with resistance.
- Support self-efficacy (patient's belief they can successfully make a change).

MET, adapted from MI principles, is a manual-based intervention designed to help patients explore ambivalence about alcohol use and develop intrinsic motivation to reduce or abstain from alcohol use [Lenz, et al. 2016]. CBT, individually or in groups, focuses on how thoughts, feelings, and behaviors influence each other and can be particularly useful for helping patients recognize and manage individual triggers for alcohol use. For CBT in an online format, see *Computer Based Training for Cognitive Behavioral Therapy (CBT4CBT)*.

Other psychologically based approaches include mindfulness and contingency management. A mindfulness approach seeks to help individuals with SUDs, including AUD, monitor for and relate differently to internal and environmental cues that trigger substance use [Bowen, et al. 2014]. Mindfulness-based relapse prevention programs have been associated with significant improvements in some alcohol-related outcomes compared with other psychosocial interventions, but

data are limited [Bowen, et al. 2014; Grant, et al. 2017]. Contingency management aims to improve SUD treatment outcomes, such as engagement in care or abstinence, by providing incentives to patients. Studies have shown that contingency management was associated with significant improvements in alcohol-related outcomes, but the approach is not feasible in most medical settings [Prendergast, et al. 2006; Benishek, et al. 2014; Dougherty, et al. 2014; Barnett, et al. 2017; McDonell, et al. 2017; Getty, et al. 2019].

Mutual support programs: *Self-Management and Recovery Training (SMART Recovery)* focuses on self-empowerment and provides mutual support through in-person group meetings and online formats. The program uses rational emotive behavior therapy, a form of CBT, to facilitate changes in thinking and thus in emotions and behaviors [Horvath and Yeterian 2012]. Some studies have shown positive alcohol-related treatment outcomes, but data are inconsistent [Beck, et al. 2017]. Some patients may find benefit in and connection to *Alcoholics Anonymous (AA)*, a 12-step, mutual-support group approach based on fellowship and the role of a higher power. A recent systematic review identified high-quality evidence indicating that AA and 12-step facilitation interventions were at least as effective in increasing abstinence and improving alcohol-related outcomes as clinical psychological interventions (e.g., MET, CBT, other 12-step program variants)[Kelly, et al. 2020]. In some AA programs, however, participants who take pharmacologic medication for AUD can be made to feel unwelcome.

Online Resources: Psychologically Based Treatment for Alcohol Use Disorder

Motivational Interviewing

- Substance Abuse and Mental Health Services Administration (SAMHSA): *Motivational Interviewing as a Counseling Style*.
- SAMHSA: *TIP 35: Enhancing Motivation for Change in Substance Use Disorder Treatment*.
- Case Western Reserve University: *MI Reminder Card ("Am I Doing This Right?") (quick guide)*.
- World Health Organization: *mhGAP Intervention Guide (mhGAP-IG) for mental, neurological, and substance use disorders for non-specialized health settings (protocols for clinical decision-making)*

Medical Management Treatment Manual

- *A Clinical Guide for Researchers and Clinicians Providing Pharmacotherapy for Alcohol Dependence (Generic Version; 2010 edition*): Designed to be used in the COMBINE study in conjunction with prescribed medication, incorporates psychosocial techniques, and provides education and tools for clinicians and patients to support abstinence and promote medication adherence.

Mutual Support Programs

- *Self-Management and Recovery Training (SMART Recovery)*
- *Moderation Management*
- *Alcoholic Anonymous*
- *New York State Alcoholics Anonymous Meeting Schedules*

Choosing a Treatment Option

Clinicians should collaborate with patients to set specific treatment goals about patient alcohol use and should document the treatment plan they agree on in the medical record [Dunn and Strain 2013; APA 2018]. Individual goals in the treatment plan may include, but are not limited to, abstinence, reduction in alcohol use, or avoiding alcohol consumption in high-risk situations (e.g., at work, before driving, when caring for children) (see the NYSDOH guideline *Harm Reduction Approach to Treatment of All Substance Use Disorders*).

If pharmacologic treatment is initiated, clinicians should schedule frequent follow-up visits to provide patients with support and encouragement and to monitor treatment response, possible adverse effects, medication adherence, and signs of continued use or return to use. If a patient continues to use alcohol, pharmacologic treatment options, except for disulfiram, can be continued. However, clinicians should discuss treatment goals and possible modifications to the treatment plan with the patient.

Adherence is essential for pharmacologic treatments to be effective, making pill burden an important practical consideration for clinicians. Treatment with acamprosate requires patients to take 2 pills thrice daily, and treatment with naltrexone requires patients to take 1 pill once daily.

The choice of psychologically based treatment for AUD is based on patient experience and preference, social factors, treatment availability, and insurance, among other individual factors.

Implementing Pharmacologic Treatment for AUD in the Primary Care Setting

☑ RECOMMENDATIONS

Managing Withdrawal Syndrome

- Before treating patients with alcohol use disorder (AUD), clinicians should assess the need for withdrawal management and (A3):
  - Manage mild to moderate withdrawal syndrome in an outpatient setting.
  - Refer patients with severe withdrawal syndrome or other complicating conditions for inpatient management.

Initiating Pharmacologic Treatment

- **PREFERRED: Acamprosate:** For use if patients have the treatment goal of either reduction of or abstinence from alcohol use.
  - Clinicians should perform serum creatinine clearance (CrCl) testing before initiating treatment with acamprosate (A3); if CrCl is between 30 and 50 mL/min or estimated glomerular filtration rate (eGFR) is between 30 and 59 mL/min/1.73 m2, clinicians should adjust the dose according to prescribing information or choose another medication. (A2)
  - **Contraindication:** Clinicians should not prescribe acamprosate for patients with a CrCl <30 mL/min or eGFR <30 mL/min/1.73 m2. (A2)
  - For the best treatment response, clinicians should initiate treatment with acamprosate as soon as a patient has abstained from alcohol use and within 7 days. (A3)
- **PREFERRED: Oral or injectable Long-Acting Extended-Release (XR) Naltrexone:** For use if patients have the treatment goal of either reduction of or abstinence from alcohol use.
  - For patients with AUD who also use opioids, clinicians should administer a naloxone challenge and confirm that the patient has no reaction to ensure that opioids have been cleared from the system (see the NYSDOH AI guideline *Treatment of Opioid Use Disorder > Implementing Opioid Use Disorder Treatment*). (A2)
  - Before initiating treatment with injectable XR naltrexone, clinicians should prescribe an oral trial of naltrexone (50 mg once daily for at least 3 days) to assure that the patient tolerates the medication. (A3)
  - Clinicians should recommend XR naltrexone if adherence to an oral regimen is a concern. (B3)
  - Because active alcohol use is not a contraindication to naltrexone, clinicians should initiate naltrexone even if patients continue to use alcohol. (A1)
  - **Contraindications:** Clinicians should not prescribe naltrexone for individuals with acute hepatitis or liver failure; individuals taking opioid analgesics; individuals currently physically dependent on opioids, including those currently maintained on opioid agonists (e.g., methadone) or partial agonists (e.g., buprenorphine); or individuals in acute opioid withdrawal. (A2)
- **ALTERNATIVE: Disulfiram:** For use if patients have the treatment goal of abstinence from alcohol use.
  - Clinicians should consider disulfiram for individuals with AUD who have not responded to or are intolerant of naltrexone or acamprosate, or who may prefer disulfiram. (A3)
  - Clinicians should advise patients that they should not take disulfiram until they have been abstinent from alcohol for 12 hours or longer. (A3)
  - Clinicians should emphasize the importance of avoiding alcohol consumption in all forms to patients taking disulfiram. (A3)
  - Clinicians should perform baseline liver function testing, including aspartate aminotransferase (AST)/alanine aminotransferase (ALT) levels, before initiating disulfiram treatment. (A3)
    - In patients with AST/ALT levels >3 to 5 times the upper limit of normal, clinicians should avoid treatment with disulfiram. (A3)
    - Clinicians should repeat liver function testing at least monthly during the first 3 months of treatment and every 3 months thereafter while the patient is taking disulfiram. (A3)

☑ RECOMMENDATIONS

  - Clinicians should discontinue disulfiram treatment in any individual with signs or symptoms of acute hepatitis or acute liver failure. (A3)
- **Contraindications:** Clinicians should not prescribe disulfiram for patients who have recent or concomitant use of metronidazole, paraldehyde, alcohol, or alcohol-containing preparations (e.g., cough syrups, tonics); coronary artery disease; recent myocardial infarction; psychoses; or signs or symptoms of acute hepatitis or acute liver failure. (A2)

- **ALTERNATIVES: Gabapentin or Topiramate:** For use if patients have the treatment goal of reducing or abstaining from alcohol use. Clinicians should consider gabapentin or topiramate for individuals with AUD who have not responded to or are intolerant of naltrexone or acamprosate, or who may prefer gabapentin or topiramate. (A3)

Managing Alcohol Withdrawal Syndrome

Before initiating AUD treatment, clinicians should determine if patients are experiencing withdrawal syndrome. If symptoms are present, clinicians should assess withdrawal severity using a validated instrument, such as the *Clinical Institute Withdrawal Assessment for Alcohol, Revised (CIWA-Ar)* or the self-completed *10-item Short Alcohol Withdrawal Scale (SAWS)*, which has been validated in the outpatient setting [Sullivan, et al. 1989; Gossop, et al. 2002; Elholm, et al. 2010; Muncie, et al. 2013].

In individuals with AUD, an abrupt cessation or significant reduction of alcohol use can precipitate an acute withdrawal syndrome within 4 to 12 hours of last alcohol use [APA 2018]. The syndrome may persist for as long as 5 days, and symptoms range from anxiety, agitation, tremor, and sympathetic nervous system activation to more serious outcomes such as seizure and delirium tremens, which can result in death if not treated [APA 2018].

In most individuals, mild to moderate alcohol withdrawal syndrome can be managed in the outpatient primary care setting [Muncie, et al. 2013] with benzodiazepines [Mayo-Smith 1997; Schaefer and Hafner 2013]. The *Prediction of Alcohol Withdrawal Severity Scale (PAWSS)* is a validated screening instrument for predicting the development of severe alcohol withdrawal. A *PAWSS* score < 4 is considered low risk for complicated alcohol withdrawal syndrome and may help to identify individuals that can be managed in the outpatient primary care setting [Maldonado, et al. 2015; Wood, et al. 2018]. For recommendations on treating alcohol withdrawal syndrome, see *The American Society of Addiction Medicine (ASAM) Clinical Practice Guideline on Alcohol Withdrawal Management*.

Gabapentin is also effective in treating common symptoms of acute and protracted alcohol withdrawal, including anxiety and sleep disturbances [Mason, et al. 2014; Mason, et al. 2018]. Gabapentin and other anticonvulsants, including carbamazepine and valproic acid, have been studied as alternatives to benzodiazepines for managing alcohol withdrawal syndrome, but data are limited. These medications have less potential for misuse and may be safer, particularly if mixed with alcohol. However, anticonvulsants do not prevent alcohol withdrawal seizures or delirium tremens. Ideally, individuals treated for alcohol withdrawal syndrome in the outpatient setting should be assessed daily until their withdrawal symptoms decrease, and the medication dosage can be reduced and eventually discontinued. For an increased likelihood of success in the outpatient setting, patients should be able to take oral medications, be committed to frequent follow-up visits, or have a relative, friend, or caregiver who can stay with them and administer medication [Blondell 2005].

Patients who have severe alcohol withdrawal symptoms should be referred to a detoxification or inpatient setting for intensive management [Myrick and Anton 1998] (see *PAWSS* for assessing the level of severity). Referral for intensive management of alcohol withdrawal may be appropriate for patients who have:

- A history of long-term heavy alcohol use.
- Acute or chronic comorbidities, including serious mental illness.
- A history of withdrawal seizures or high risk of delirium tremens.
- Concurrent use of other drugs.

Initiating Pharmacologic Treatment

Acamprosate (Preferred)

Clinicians should initiate treatment with acamprosate as soon as the individual has abstained from alcohol use (within 7 days) for the best treatment response. Acamprosate can be initiated if the individual is still actively using alcohol, but the efficacy of treatment during active alcohol use is unknown.

Because acamprosate is excreted through the kidneys, clinicians should measure CrCl before starting treatment. Dose reduction may be necessary for patients with CrCl between 30 and 50 mL/min or eGFR between 30 and 59 mL/min/1.73 m^2. Acamprosate may be a good option for patients with AUD who have significant hepatic dysfunction because it is not metabolized through the liver and has no reported risk of hepatotoxicity.

Acamprosate has been most effective as an AUD treatment in individuals with high levels of motivation [Jonas, et al. 2014]. Clinicians should work with patients to assess and enhance motivation (e.g., via motivational interviewing). Acamprosate should be initiated as soon as possible after alcohol withdrawal (within 7 days) and may be maintained if the individual continues or returns to alcohol use.

Induction and maintenance: Oral acamprosate is typically started and continued as 3 doses daily, two 333 mg tablets for each dose for a total of 1998 mg daily.

Adverse effects: Acamprosate is generally well tolerated; the most frequently reported adverse effect in clinical trials was diarrhea [Lhuintre, et al. 1985; Chick, et al. 2000b; Sinclair, et al. 2016]. If diarrhea is severe, a temporary dose reduction may be beneficial [Lhuintre, et al. 1985; Chick, et al. 2000a; Sinclair, et al. 2016].

Naltrexone (Preferred)

Active alcohol use is not a contraindication to initiating treatment with naltrexone (oral and XR formulations).

In clinical studies, high adherence to oral naltrexone, defined as pills taken on more than 80% to 90% of days, was necessary to achieve significant treatment effects [Chick, et al. 2000a; Srisurapanont and Jarusuraisin 2005]. Assessing and supporting a patient's ability to adhere to oral naltrexone before starting treatment (e.g., via motivational interviewing) is essential. Engaging family members or others to assist with adherence to oral naltrexone can be helpful.

XR naltrexone may improve adherence compared to oral naltrexone [Hartung, et al. 2014]. XR naltrexone is administered as a 380 mg intramuscular gluteal injection every 28 days (alternating buttocks for each subsequent injection). When an XR naltrexone injection is delayed beyond 28 days, clinicians can provide the patient with a prescription for daily oral naltrexone (50 mg daily) to take until they can receive the injection.

Naltrexone is contraindicated in individuals with acute hepatitis or liver failure; therefore, baseline assessment of liver function should be performed before treatment initiation. Naltrexone is a preferred treatment option in patients with AST/ALT levels lower than 3 to 5 times the upper limit of normal [Turncliff, et al. 2005; Kwo, et al. 2017]. Clinicians can also consider performing follow-up liver tests 4 to 12 weeks after initiating naltrexone treatment [Lucey, et al. 2008]. The extent of liver abnormalities may guide continued testing or referral to an experienced liver specialist.

Induction and maintenance (oral): The recommended induction and maintenance dose of oral naltrexone is 50 mg daily. However, a dose of 100 mg daily was used and well tolerated in the large COMBINE trial [Anton, et al. 2018], so a dose increase may be considered.

Induction and maintenance (injectable): The recommended induction dose is 50 mg oral naltrexone once daily for at least 3 days to assure that the patient tolerates the medication. A maintenance dose is 380 mg naltrexone administered as an intragluteal injection every 28 days.

Individuals with AUD who also use opioids should be abstinent from opioids for approximately 7 to 14 days before initiating XR naltrexone, which is considered an alternative treatment for OUD (see the NYSDOH AI guideline *Treatment of Opioid Use Disorder > Implementing Opioid Use Disorder Treatment*). Clinicians should confirm the length of time since last opioid use by performing a naloxone challenge. Administer a single intranasal dose (2.0 mg/0.1 cc) of naloxone and confirm the response. In individuals with recent opioid use, this may precipitate opioid withdrawal. If a patient is already taking oral naltrexone, a naloxone challenge is not necessary.

Adverse Events: Oral and XR naltrexone are generally well tolerated. The more common adverse events include gastrointestinal symptoms, such as nausea , vomiting, abdominal pain, diarrhea, and dizziness [FDA 2010, 2013].

Gastrointestinal adverse events associated with naltrexone may be more common among women than among men [Herbeck, et al. 2016]. If an individual experiences adverse events with oral naltrexone, clinicians can consider a reduced dose of 25 mg [Anton 2008].

XR naltrexone can cause pain or hardening of soft tissue at the injection site. The potential for bleeding at the injection site in individuals who have coagulopathy or are taking anticoagulants should be considered. Sufficient adipose tissue is required for injection and may be difficult in an individual who is cachectic.

Disulfiram (Alternative)

Disulfiram is contraindicated in individuals who are actively using alcohol. Clinicians should consider it a treatment option only for individuals with a clear goal of abstaining from alcohol. If alcohol is consumed within 12 hours of taking disulfiram, the accumulation of acetaldehyde produces a severe physiologic response. It is essential to educate patients about avoiding medications or common products that contain alcohol, such as cough and cold medicines, mouthwashes, tonics, sauces, vinegar, and other food or skin products, because they may precipitate this adverse reaction.

Disulfiram does not reduce an individual's cravings for alcohol; instead, it provides an adverse reaction to alcohol use. Thus, motivation and consistent adherence are required for disulfiram to be effective as a deterrent to alcohol use. In clinical trials, individuals who chose disulfiram as their preferred treatment and were highly adherent or were receiving disulfiram under supervision achieved the greatest success [Chick, et al. 1992; O'Farrell, et al. 1995; Johnson 2008; Laaksonen, et al. 2008].

→ GOOD PRACTICES

- Emphasize that consumption of ANY alcohol during treatment with disulfiram can result in flushing, throbbing in head and neck, respiratory difficulty, nausea, copious vomiting, sweating, thirst, chest pain, palpitations, dyspnea, hyperventilation, tachycardia, hypotension, syncope, marked uneasiness, weakness, vertigo, blurred vision, and confusion.
- Inform patients that adverse reactions to alcohol ingestion may occur for up to 14 days after stopping disulfiram treatment.
- Advise patients to carry a wallet card or wear a medication bracelet that states they are taking disulfiram so this information will be available to emergency personnel in case of a severe adverse reaction [NIAAA 2016].
- Educate patients taking disulfiram that alcohol may be found in cough and cold medicines, mouthwashes, tonics, sauces, vinegars, and other food or skin products.

Disulfiram has been associated with mild increases in hepatic enzymes in approximately 25% of individuals taking the medication [Bjornsson, et al. 2006]. Acute and potentially fatal hepatotoxicity is very rare (1 per 10,000 to 30,000 years of disulfiram treatment) [Bjornsson, et al. 2006]. Clinicians should perform baseline liver function testing, including AST/ALT tests, before initiating treatment with disulfiram and consider initiating disulfiram if AST/ALT levels are lower than 3 to 5 times the upper limit of normal [Kwo, et al. 2017]. It may be useful for clinicians to obtain follow-up liver test results within 1 month of initiating treatment. The extent of liver abnormalities may guide continued testing or referral to a liver specialist. In addition, disulfiram is not considered safe in individuals with serious medical comorbidities (e.g., cardiovascular disease) or serious mental illnesses (e.g., psychotic disorders) [FDA 2017a].

Induction and maintenance: The initial dose of disulfiram is up to 500 mg once daily for 1 to 2 weeks. The recommended maintenance dose of disulfiram is 250 mg daily (range, 125 mg to 500 mg).

Adverse events: Consuming alcohol while taking disulfiram can result in the adverse reactions described in the *Good Practice b*ox above. Because disulfiram is contraindicated in patients with coronary artery disease or recent myocardial infarction, it may be appropriate to assess cardiac function before starting treatment with disulfiram. Disulfiram is not recommended for patients with seizure disorders or a history of psychosis. Caution should be taken in prescribing disulfiram to patients who have a family history of psychosis [FDA 2017a].

Gabapentin (Alternative)

At doses of up to 1800 mg daily, gabapentin is safe and well tolerated in individuals with AUD [Mason, et al. 2014; Mason, et al. 2018]. Abstinence from alcohol is not a requirement for initiating gabapentin treatment; there are no adverse interactions reported when alcohol and gabapentin are consumed at the same time [Myrick, et al. 2007]. Gabapentin has

been increasingly associated with opioid-related overdose deaths; caution is required when prescribing gabapentin for individuals with comorbid AUD and opioid use disorder [Chiappini and Schifano 2016].

Gabapentin is excreted through the kidneys, and clinicians may consider performing tests for serum creatinine levels, particularly when administering high doses of gabapentin. Dose reduction may be necessary for patients with reduced renal function. Because gabapentin is not metabolized through the liver and has no reported risk of hepatotoxicity, it may be a good option for individuals with AUD who have significant hepatic dysfunction.

→ KEY POINTS

- Because gabapentin can induce a sense of euphoria [Mersfelder and Nichols 2016; Smith, et al. 2016] when taken in combination with other substances, especially opioids, benzodiazepines, or alcohol, there is the potential for misuse.
- Individuals may take gabapentin for recreational purposes, to control mood or anxiety, to intensify the effects of substance use disorder medication, or for intentional self-harm.
- If there is a strong concern about gabapentin misuse or diversion, clinicians may want to schedule monthly or more frequent follow-up visits and medication counts [Mersfelder and Nichols 2016; Smith, et al. 2016].

Induction and maintenance: The initial dose of gabapentin is 300 mg once daily, with increases in increments of 300 mg every 1 to 2 days based on response and tolerability. The maintenance dose is individualized and generally divided into 3 doses per day**.** Based on studies of gabapentin for the treatment of other conditions (e.g., epilepsy, postherpetic neuralgia), maintenance doses up to 2,400 mg or 3,600 mg per day, divided into 3 doses, can be considered [FDA 2017b]**.**

Adverse events: Common adverse events include headache, insomnia, fatigue, muscle aches, and gastrointestinal complaints. In clinical trials, these events were mild to moderate, did not result in drug discontinuation, and were not significantly different from adverse effects reported with placebo [Mason, et al. 2018].

Topiramate (Alternative)

Clinicians can offer topiramate to patients with moderate-to-severe AUD (*Diagnostic and Statistical Manual of Mental Disorders–5* criteria) who have a goal of reducing alcohol use or achieving abstinence. Abstinence from alcohol is not a requirement for initiating treatment.

Induction and maintenance doses: The initial dose of topiramate is 25 mg once daily, with increases in increments of 50 mg once every 7 days. The maintenance dose ranges from 200 mg to 400 mg daily, divided into 2 doses [Johnson, et al. 2003; Kranzler, et al. 2014; Knapp, et al. 2015]. In patients with moderate-to-severe renal impairment, a 50% dose reduction is advised [Perucca 1997; Guerrini and Parmeggiani 2006].

Adverse events: Adverse effects that occurred in more than 10% of study subjects include paresthesia [Fujii, et al. 1993; Spitzer, et al. 2002; Swietach, et al. 2003] and cognitive impairment [Gomer, et al. 2007]. These effects were mostly observed in the dose titration phase and often resolved with continued treatment. Rare adverse effects include increased rate of renal calculi (2- to 4-fold) [Welch, et al. 2006], oligohidrosis [Cerminara, et al. 2006; Ma, et al. 2007], acute visual disturbances, and myopia and acute angle-closure glaucoma [Shank and Maryanoff 2008].

Table 1: Pharmacologic Treatment of Alcohol Use Disorder in Nonpregnant Adults [a]

Medication [b]	**Dosage**	**Considerations for Use**
Preferred Medications		
Acamprosate oral (Campral)	**Initial and maintenance:** 666 mg 3 times per day.	• **Contraindication:** Patients with CrCl ≤30 mL/min or eGFR ≤30 mL/min/1.73 m^2. See package insert for dose adjustments based on CrCl.
Naltrexone oral (Revia)	**Initial and maintenance:** 50 mg once daily. If adverse events occur, clinicians can consider a reduced dose of 25 mg once daily.	• **Contraindications:** Acute hepatitis or liver failure, concomitant use of opioid analgesics or opioid agonists (e.g., methadone or buprenorphine), acute opioid withdrawal. • Abstinence from alcohol is not required for treatment. • Abstinence from opioids is required for treatment. For patients who use alcohol and opioids, see recommendations in the

Table 1: Pharmacologic Treatment of Alcohol Use Disorder in Nonpregnant Adults [a]		
Medication [b]	**Dosage**	**Considerations for Use**
XR Naltrexone, long-acting injectable (Vivitrol)	**Initial:** 50 mg oral naltrexone once daily for at least 3 days. **Maintenance:** 380 mg intragluteal injection every 28 days.	NYSDOH AI guideline *Treatment of OUD > Implementing OUD Treatment in the Primary Care Setting > Naltrexone*. • If possible, perform liver function testing (including AST/ALT testing) at baseline and within 12 weeks of initiating treatment. • Discontinue naltrexone in the event of symptoms or signs of impaired liver function. • Recommend the injectable formulation for patients who have problems with adherence to the oral regimen.
Alternative Medications		
Disulfiram oral (Antabuse)	**Initial and maintenance:** 500 mg once daily for 1 to 2 weeks. Reduce to 250 mg once daily.	• **Contraindications:** Recent or concomitant use of metronidazole, paraldehyde, alcohol, or alcohol-containing preparations (e.g., cough syrups, tonics); coronary artery disease; recent myocardial infarction; psychoses; or signs or symptoms of acute hepatitis or acute liver failure. For all contraindications, see package insert. • Use only in patients who want to completely abstain from alcohol. • Inform patients of the disulfiram-alcohol reaction [c]; reinforce complete abstinence from any form of alcohol. • Advise patients to initiate disulfiram only after 12 hours of abstinence. • Perform baseline liver testing before initiating disulfiram treatment. • In patients with AST/ALT levels >3 to 5 times the upper limit of normal, avoid treatment with disulfiram. • Repeat liver function testing at least monthly during the first 3 months of treatment and every 3 months thereafter while patient is taking disulfiram.
Gabapentin oral (multiple brands)	**Initial:** 300 mg once daily. **Titrate:** Increase in increments of 300 mg. **Maintenance:** Up to 3,600 mg daily, divided in 3 doses; dose is based on response and tolerance.	• **Caution:** Gabapentin can be used alone for psychoactive effect or in combination with other substances, including opioids, benzodiazepines, and alcohol, to intensify the effects.
Topiramate oral (multiple brands)	**Initial:** 25 mg once daily. **Titrate:** Increase dose by 50 mg increments each week to a maximum of 400 mg daily administered in 2 divided doses. **Maintenance:** 200 to 400 mg daily divided into 2 doses.	• A dose reduction by half is recommended for adult patients with CrCl ≤70 mL/min or eGFR ≤70 mL/min/1.73 m^2. See package insert for full *prescribing information*.

Abbreviation key: AST/ALT, aspartate aminotransferase/alanine aminotransferase; CrCl, creatinine clearance; eGFR, estimated glomerular filtration rate.

a. For treatment of pregnant individuals with AUD, see *American Psychiatric Association Practice Guideline for the Pharmacological Treatment of Patients With Alcohol Use Disorder, Statement 14: Pharmacotherapy in Pregnant or Breastfeeding Women.*

b. Consult package insert for full prescribing information for each medication.

Table 1: Pharmacologic Treatment of Alcohol Use Disorder in Nonpregnant Adults [a]		
Medication [b]	**Dosage**	**Considerations for Use**
c. Concomitant use of disulfiram and alcohol, even small amounts, can result in the following adverse effects: flushing, throbbing in head and neck, respiratory difficulty, nausea, copious vomiting, sweating, thirst, chest pain, palpitations, dyspnea, hyperventilation, tachycardia, hypotension, syncope, marked uneasiness, weakness, vertigo, blurred vision, and confusion. Severe reactions may result in respiratory depression, cardiovascular collapse, arrhythmias, myocardial infarction, acute congestive heart failure, unconsciousness, convulsions, and death.		

All Recommendations

☑ All RECOMMENDATIONS: Treatment of Alcohol Use Disorder

Treatment Options

- Clinicians should inform patients with alcohol use disorder (AUD) about all available pharmacologic and psychologically based treatment options and all available treatment settings, including outpatient primary care and addiction specialty treatment (intensive outpatient, inpatient, and residential treatments). (A3)

Choosing a Treatment Option

- Clinicians should recommend pharmacologic treatment for individuals with moderate-to-severe AUD (see *Table 1: Pharmacologic Treatment of Alcohol Use Disorder in Nonpregnant Adults*). (A1)
  - Clinicians should recommend oral acamprosate or oral or injectable extended-release (XR) naltrexone as the preferred medications for treating AUD. (A1)
- Clinicians and patients should choose a pharmacologic agent based on: (A3)
  - Evidence-based recommendations.
  - Ease of administration.
  - Available formulations.
  - Adverse effects.
  - Presence of medical conditions (e.g., hepatic or renal disease, conditions that require treatment with opioids).
  - Comorbid psychiatric conditions (e.g., depression, anxiety) and/or substance use disorders (e.g., opioid use disorder, tobacco use disorder).
  - Presence of specific features of AUD (e.g., craving).
  - Patient preference.
- Clinicians should recommend psychologically based treatment for individuals with AUD. (A1)

Managing Withdrawal Syndrome

- Before treating patients with alcohol use disorder (AUD), clinicians should assess the need for withdrawal management and (A3):
  - Manage mild to moderate withdrawal syndrome in an outpatient setting.
  - Refer patients with severe withdrawal syndrome or other complicating conditions for inpatient management.

Initiating Pharmacologic Treatment

- **PREFERRED: Acamprosate:** For use if patients have the treatment goal of either reduction of or abstinence from alcohol use.
  - Clinicians should perform serum creatinine clearance (CrCl) testing before initiating treatment with acamprosate (A3); if CrCl is between 30 and 50 mL/min or estimated glomerular filtration rate (eGFR) is between 30 and 59 mL/min/1.73 m2, clinicians should adjust the dose according to prescribing information or choose another medication. (A2)
  - **Contraindication:** Clinicians should not prescribe acamprosate for patients with a CrCl <30 mL/min or eGFR <30 mL/min/1.73 m2. (A2)

☑ All RECOMMENDATIONS: Treatment of Alcohol Use Disorder

- For the best treatment response, clinicians should initiate treatment with acamprosate as soon as a patient has abstained from alcohol use and within 7 days. (A3)

- **PREFERRED: Oral or injectable Long-Acting Extended-Release (XR) Naltrexone:** For use if patients have the treatment goal of either reduction of or abstinence from alcohol use.
  - For patients with AUD who also use opioids, clinicians should administer a naloxone challenge and confirm that the patient has no reaction to ensure that opioids have been cleared from the system (see the NYSDOH AI guideline *Treatment of Opioid Use Disorder > Implementing Opioid Use Disorder Treatment*). (A2)
  - Before initiating treatment with injectable XR naltrexone, clinicians should prescribe an oral trial of naltrexone (50 mg once daily for at least 3 days) to assure that the patient tolerates the medication. (A3)
  - Clinicians should recommend XR naltrexone if adherence to an oral regimen is a concern. (B3)
  - Because active alcohol use is not a contraindication to naltrexone, clinicians should initiate naltrexone even if patients continue to use alcohol. (A1)
  - **Contraindications:** Clinicians should not prescribe naltrexone for individuals with acute hepatitis or liver failure; individuals taking opioid analgesics; individuals currently physically dependent on opioids, including those currently maintained on opioid agonists (e.g., methadone) or partial agonists (e.g., buprenorphine); or individuals in acute opioid withdrawal. (A2)
- **ALTERNATIVE: Disulfiram:** For use if patients have the treatment goal of abstinence from alcohol use.
  - Clinicians should consider disulfiram for individuals with AUD who have not responded to or are intolerant of naltrexone or acamprosate, or who may prefer disulfiram. (A3)
  - Clinicians should advise patients that they should not take disulfiram until they have been abstinent from alcohol for 12 hours or longer. (A3)
  - Clinicians should emphasize the importance of avoiding alcohol consumption in all forms to patients taking disulfiram. (A3)
  - Clinicians should perform baseline liver function testing, including aspartate aminotransferase (AST)/alanine aminotransferase (ALT) levels, before initiating disulfiram treatment. (A3)
    - In patients with AST/ALT levels >3 to 5 times the upper limit of normal, clinicians should avoid treatment with disulfiram. (A3)
    - Clinicians should repeat liver function testing at least monthly during the first 3 months of treatment and every 3 months thereafter while the patient is taking disulfiram. (A3)
    - Clinicians should discontinue disulfiram treatment in any individual with signs or symptoms of acute hepatitis or acute liver failure. (A3)
  - **Contraindications:** Clinicians should not prescribe disulfiram for patients who have recent or concomitant use of metronidazole, paraldehyde, alcohol, or alcohol-containing preparations (e.g., cough syrups, tonics); coronary artery disease; recent myocardial infarction; psychoses; or signs or symptoms of acute hepatitis or acute liver failure. (A2)
- **ALTERNATIVES: Gabapentin or Topiramate:** For use if patients have the treatment goal of reducing or abstaining from alcohol use. Clinicians should consider gabapentin or topiramate for individuals with AUD who have not responded to or are intolerant of naltrexone or acamprosate, or who may prefer gabapentin or topiramate. (A3)

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