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

Treatment of Alcohol Use Disorder

Updates, Authorship, and Related Guidelines

Date of current publication	October 2, 2023
Highlights of changes, additions, and updates in the October 2, 2023 edition	General update including trends in the prevalence of alcohol use disorder in the United States, emerging treatment strategies, current evidence for treatment recommendations, and the importance of harm reduction approach to treatment
Intended users	Primary care clinicians and other practitioners in New York State who provide medical care to adult patients who have alcohol use disorder
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Author and writing group conflict of interest disclosures	None
Date of original publication	July 2020
Committee	Substance Use Guidelines Committee
Developer and funder	New York State Department of Health AIDS Institute (NYSDOH AI)
Development process	See Supplement: Guideline Development and Recommendation Ratings
Related NYSDOH AI guidelines	• Substance Use Harm Reduction in Medical Care • Substance Use Screening, Risk Assessment, and Use Disorder Diagnosis in Adults • Substance Use Disorder Treatment in Pregnant Adults • Treatment of Opioid Use Disorder

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Contents

Purpose 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 provide clinical guidance for practitioners who provide medical care for adults in New York State.

This guideline aims to:

- Increase clinicians' awareness of the risks associated with AUD of any severity and the benefits of diagnosing and treating AUD in adults
- Increase clinicians' knowledge of available evidence-based treatments for AUD and withdrawal management and increase the availability of AUD treatment in ambulatory care settings in New York State
- Promote a harm reduction approach to AUD treatment through implementation of practical strategies for reducing the negative consequences associated with alcohol use (see NYSDOH AI guideline Substance Use Harm Reduction in Medical Care)

AUD is a medical condition characterized by an impaired ability to stop or control alcohol use despite adverse social, occupational, or health consequences. AUD, which has been referred to as alcohol abuse, alcohol dependence, alcohol addiction, and alcoholism, encompasses all and can be mild, moderate, or severe based on the number of *Diagnostic and Statistical Manual of Mental Disorders-5* criteria met [NIAAA(a) 2023]. The 2021 National Survey on Drug Use and Health in the United States reported that an estimated 28.6 million individuals aged 18 years or older in the United States had AUD in the past year [SAMHSA 2023]. Among people aged 12 years or older with AUD in the past year, 0.9% received pharmacologic AUD treatment during that period.

A wide range of negative health outcomes are associated with alcohol use in individuals with AUD or unhealthy alcohol use that does not meet the criteria for AUD. These include an increased risk of liver disease, heart disease, depression, stroke, and stomach bleeding; cancers of the oral cavity, esophagus, larynx, pharynx, colon, and rectum; difficulty managing diabetes, high blood pressure, pain, and sleep disorders; increased risk of drowning; and injuries from violence, falls, and motor vehicle crashes [NIAAA(a) 2023; Bagnardi, et al. 2015; Grewal and Viswanathen 2012; Taylor and Rehm 2012; Taylor, et al. 2010; Baan, et al. 2007; Cherpitel 2007; Driscoll, et al. 2004].

In the United States, among individuals aged 16 years and older, the alcohol use-associated death rate increased by 50.9% between 1999 and 2017. In 2017, 2.6% of approximately 2.8 million deaths in the United States were associated with alcohol use, with liver disease and alcohol overdose or overdose with alcohol and other drugs accounting for nearly 50% [White, et al. 2020]. During the COVID-19 pandemic, observed AUD-related mortality rates were higher than projected rates, by 24.79% in 2020 and 21.95% in 2021, with the highest increase in AUD mortality observed in the youngest age group (25 to 44 years) [Yeo, et al. 2022].

Role of primary care clinicians: Primary care clinicians in New York State can play an essential role in identifying and treating unhealthy alcohol use and AUD in their patients. The focus of this guideline is AUD treatment. Despite the prevalence of AUD and associated risks and the availability of effective outpatient treatment, AUD treatment declined from 2008 to 2017 [Larsen, et al. 2022]. Because primary care may lend itself to long-term relationships, this treatment setting is ideal for managing AUD as a chronic health condition.

Treatment Considerations

☑ RECOMMENDATIONS

Who to Treat

- Clinicians should recommend and offer pharmacologic treatment to individuals with moderate or severe AUD. (A1) See the guideline section Preferred Pharmacologic Treatment.
- Clinicians should recommend behavioral treatment for individuals with AUD and refer as appropriate. (A1) See the guideline section Behavioral Treatment.

Treatment Goals and Selection

- Clinicians should inform patients with AUD about all available pharmacologic and behavioral treatment options and all available treatment settings, including outpatient primary care and addiction specialty treatment (intensive outpatient, inpatient, and residential treatments). (A3)
- Clinicians should engage in shared decision-making with patients to set specific treatment goals, including harm reduction. (A3)
- Clinicians and patients should choose a pharmacologic agent based on evidence-based recommendations; patient preference; current level of alcohol use [a]; experience of cravings; risk of withdrawal syndrome; available support; available formulations; potential adverse effects; dosing schedules (adherence may be increased with once-daily dosing); medical or psychiatric comorbidities that may preclude use of a specific agent or require increased monitoring, including hepatic or renal dysfunction; depression or anxiety; a concomitant SUD; and concomitant opioid use or misuse. (A3)

Alcohol Withdrawal Syndrome

- Before initiating AUD treatment, clinicians should assess the need for withdrawal management. (A3) Mild-to-moderate withdrawal syndrome can be managed in the outpatient setting; severe withdrawal syndrome or other complicating conditions should be referred for inpatient management [b].

Follow-Up

- If a patient taking acamprosate or naltrexone for AUD continues or resumes alcohol use, the clinician should continue to prescribe the medication, advise the patient to continue treatment, and discuss possible modifications to treatment goals. (A3)

Abbreviations: AUD, alcohol use disorder; SUD, substance use disorder.

Notes:

a. Disulfiram is contraindicated in individuals who are actively using alcohol. See the guideline section Alternative Pharmacologic Treatment > Disulfiram.
b. See the American Society of Addiction Medicine (ASAM) Clinical Practice Guideline on Alcohol Withdrawal Management 2020.

A combination of pharmacologic and behavioral treatment is the standard of care for patients with AUD [Ray, et al. 2020; Anton, et al. 2006]. Systematic reviews and meta-analyses have demonstrated that both approaches, alone and in combination, can effectively reduce the frequency and quantity of alcohol use [Bahji, et al. 2022; Ray, et al. 2020; Magill, et al. 2019; DiClemente, et al. 2017; Jonas, et al. 2014; Anton, et al. 2006]. A retrospective cohort study found that pharmacologic treatment for AUD was associated with reduced incidence and progression of alcohol-associated liver disease [Vannier, et al. 2022].

Treatment Goals

As with other chronic conditions, AUD treatment goals should be individualized and are likely to change over time. Clinicians and patients should 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.

A traditional goal of AUD treatment is long-term cessation of alcohol use, which may not be achievable for many individuals. Alternative treatment goals can lead to substantial improvements in the health and lives of those with AUD [Witkiewitz, et al. 2021]. The National Institute on Alcohol Abuse and Alcoholism research definition of recovery from AUD is a reflection of the shift to a non-abstinence-based AUD treatment approach:

> "Recovery is a process through which an individual pursues both remission from AUD and cessation from heavy drinking. An individual may be considered 'recovered' if both remission from AUD and cessation from heavy drinking are achieved and maintained over time. For those experiencing alcohol-related functional impairment and other adverse consequences, recovery is often marked by the fulfillment of basic needs, enhancements in social support and spirituality, and improvements in physical and mental health, quality of life, and other dimensions of well-being. Continued improvement in these domains may, in turn, promote sustained recovery." [NIAAA(b) 2023]

Harm reduction treatment goals may include the following:

- Staying engaged in care, which can facilitate prevention, diagnosis, and treatment of other conditions
- Reducing alcohol use
- Reducing high-risk behaviors (e.g., driving while intoxicated, engaging in condomless sex while drinking, using other substances while drinking, engaging in violent behavior toward intimate partners and others)
- Improving quality of life and other social indicators, such as employment, stable housing, and risk of incarceration
- Improving mental health

Treatment Selection

Clinicians should inform patients with AUD about all available pharmacologic and behavioral treatment options and all available treatment settings. The choice of treatment(s) is based on shared decision-making that considers individual goals, needs, and preferences; evidence-based treatment recommendations; resources; and other factors.

Pharmacologic treatment: Currently, 3 medications are approved by the U.S. Food and Drug Administration 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 (see guideline sections Preferred Pharmacologic Treatment and Alternative Pharmacologic Treatment). Recent study results suggest that treatment with hallucinogenic (e.g., psilocybin) and dissociative (e.g., ketamine) agents in conjunction with psychotherapy may decrease the percentage of heavy drinking days and increase days abstinent from alcohol [Bogenschutz, et al. 2022; Calleja-Conde, et al. 2022; Garel, et al. 2022; Grabski, et al. 2022]. More research is needed to confirm the benefits of these treatments for AUD.

Adherence is essential for pharmacologic treatment to be effective, making pill burden an important practical consideration for clinicians. Acamprosate is dosed 3 times daily, with 2 pills required for each dose, oral naltrexone is formulated for single-tablet once-daily dosing, and XR naltrexone is administered every 28 days.

Behavioral treatment: Behavioral treatment is typically delivered in a specialty addiction treatment program. The most commonly used and effective AUD interventions include assessment, personalized feedback, motivational interviewing (MI), goal setting, planning and review of homework, problem-solving skills, and relapse prevention and management [Nadkarni, et al. 2023]. For a discussion of MI, contingency management, cognitive behavioral therapy, and other behavioral treatments for AUD, see the guideline section Behavioral Treatment.

Alcohol Withdrawal Syndrome

Before initiating AUD treatment, clinicians should determine if patients are or are at risk of 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 [Muncie, et al. 2013; Elholm, et al. 2010; Gossop, et al. 2002; Sullivan, et al. 1989].

In individuals with AUD, abruptly ceasing or significantly reducing alcohol use can precipitate acute withdrawal syndrome within 4 to 12 hours of last alcohol use [APA 2017]. The syndrome may persist for as long as 5 days, with symptoms ranging from mild (anxiety, agitation, tremor, and sympathetic nervous system activation) to severe and life-threatening (seizure and delirium tremens) if untreated [APA 2017]. In most individuals, mild-to-moderate alcohol withdrawal syndrome can be managed in the outpatient primary care setting [Muncie, et al. 2013] with benzodiazepines [Schaefer and Hafner 2013; Mayo-Smith 1997]. 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 identify individuals that can be treated in the outpatient primary care setting [Wood, et al. 2018; Maldonado, et al. 2015]. For recommendations on treating alcohol withdrawal syndrome, see the American Society of Addiction Medicine (ASAM) Clinical Practice Guideline on Alcohol Withdrawal Management 2020.

Gabapentin effectively treats common symptoms of acute and protracted alcohol withdrawal, including anxiety and sleep disturbances [Mason, et al. 2018; Mason, et al. 2014]. Gabapentin and other anticonvulsants, including carbamazepine and valproic acid, have been studied as alternatives to benzodiazepines for managing alcohol withdrawal syndrome [Fluyau, et al. 2023; Anton, et al. 2020; Barrons and Roberts 2010; Myrick, et al. 2009; Bonnet, et al. 1999]. These medications have less potential for misuse and may be safer, particularly if mixed with alcohol. Ideally, individuals treated for alcohol withdrawal syndrome in the outpatient setting are assessed daily until their withdrawal symptoms decrease, and the medication dosage is reduced and eventually discontinued. To increase the 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 experience 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 or unstable medical or psychiatric comorbidities that require a high level of monitoring (e.g., severe coronary artery disease, hepatic or renal impairment, dementia, or risk for delirium)
- A history of withdrawal seizures or high risk of delirium tremens
- A concurrent SUD or use of other drugs, particularly benzodiazepines and opioids

See the American Society of Addiction Medicine (ASAM) Alcohol Withdrawal Management Guideline for detailed recommendations regarding levels of care.

Follow-Up

Frequent follow-up visits allow clinicians to provide support and encouragement and monitor treatment response, adverse effects, medication adherence, and signs of continued alcohol use or return to use. Follow-up within 2 weeks of treatment initiation allows tailoring of the treatment plan to individual needs (e.g., change in dose of pharmacologic treatment, addition of support services). As patients stabilize on treatment, monthly or at least quarterly follow-up allows for ongoing evaluation to ensure that treatment goals are being met.

Behavioral Treatment

☑ RECOMMENDATION

Behavioral Treatment

- Clinicians should recommend behavioral treatment for patients with alcohol use disorder (AUD) and refer as appropriate. (A1) The type of treatment is based on the individual patient's experience and preference, social factors, treatment availability, and insurance, among other factors.

Many studies support the effectiveness of motivational interviewing (MI), motivational enhancement therapy (MET), and cognitive behavioral therapy (CBT) for treating individuals with AUD [Miller 2018; DiClemente, et al. 2017; Lenz, et al. 2016; Lundahl, et al. 2013; Smedslund, et al. 2011; Lundahl, et al. 2010; Magill and Ray 2009], including studies conducted in the primary care setting [VanBuskirk and Wetherell 2014; Lundahl, et al. 2013; Stecker, et al. 2012]. A systematic review and meta-analysis found that combining evidence-based behavioral intervention and pharmacologic treatment was associated with better AUD treatment outcomes than clinical management or nonspecific counseling services [Ray, et al. 2020].

MI, MET, CBT, and other approaches have been incorporated into many interventions for AUD treatment. Variables in studies of behavioral 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 the type of approach, duration and number of sessions, type and training of the clinician delivering the intervention, treatment setting, mode of delivery (in-person or computerized), individual or group intervention, 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 act toward resolving them, and it can be helpful for clinicians to understand and use an MI-informed approach when discussing alcohol use and AUD treatment plans with patients. The overall goal of MI is to increase the individual's intrinsic motivation to facilitate change, and the method is particularly useful for those who are ambivalent about changing behavior or who are reluctant to change [Miller and Rollnick 2002]. This technique emphasizes patients' autonomy while providing a safe space for collaboration and consistent engagement to enhance motivation for change. The MI approach also helps clinicians assess the patients' readiness to change behavior and use that level as a starting point for counseling or treatment.

Box 1: Key Principles of Motivational Interviewing

- Express empathy and practice reflective listening.
- Avoid arguing and confrontation.
- Develop the discrepancy between a patient's goals or values and their current behavior.
- Adjust to the patient's resistance rather than opposing it directly.
- Support optimism and 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 behavioral approaches include mindfulness and contingency management (CM). 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 [Grant, et al. 2017; Bowen, et al. 2014]. CM aims to improve SUD treatment outcomes, such as engagement in care or abstinence, by providing patient incentives. In studies, contingency management has been associated with significant improvements in alcohol-related outcomes, but providing a CM intervention in a real-world medical setting has been difficult [Getty, et al. 2019; Barnett, et al. 2017; McDonell, et al. 2017; Benishek, et al. 2014; Dougherty, et al. 2014; Prendergast, et al. 2006].

To date, the U.S. Food and Drug Administration has approved a prescription CBT app for use as an adjunct treatment for alcohol and other substance use disorders [Maricich, et al. 2022; FDA(a) 2017], but availability is uncertain. This mobile system includes a patient app and a clinician dashboard and is intended to be used in conjunction with outpatient therapy and a CM system. Mobile apps (SoberDiary) and low-cost breathalyzer devices can be purchased by individuals, and studies have shown combining mobile apps with remote breathalyzers that provide CM is an effective strategy for reducing alcohol use [Oluwoye, et al. 2020; Koffarnus, et al. 2018; You, et al. 2017; Alessi and Petry 2013]. As a new format for treatment, app-based CM has some promising results but has not yet been widely adopted into real-world settings.

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 the data are inconsistent [Beck, et al. 2017]. Some patients may benefit from 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 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]. Mutual-support groups can complement pharmacologic and other treatment modalities.

◊ RESOURCES

Motivational Interviewing	Medical Management Treatment Manual	Mutual-Support Programs
• Substance Abuse and Mental Health Services Administration: TIP 35: Enhancing Motivation for Change in Substance Use Disorder Treatment: Updated 2019 • Case Western Reserve University: MI Reminder Card (Am I Doing This Right?)	• A Clinical Research Guide for Medically Trained Clinicians Providing Pharmacotherapy as Part of the Treatment for Alcohol Dependence: 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	• Self-Management and Recovery Training (SMART Recovery) • Moderation Management • Alcoholics Anonymous • New York State Alcoholics Anonymous Meeting Schedule Portal

Preferred Pharmacologic Treatment

☑ RECOMMENDATIONS

Preferred Pharmacologic Treatment

- Clinicians should recommend oral acamprosate or oral or injectable XR naltrexone as the preferred medication for AUD treatment. (A1) See Table 1: Preferred Pharmacologic Treatment of Alcohol Use Disorder in Nonpregnant Adults.

Acamprosate

- For the best treatment response, clinicians should initiate treatment with acamprosate as soon as patients have abstained from alcohol use and within 7 days. (A3)
- Clinicians should perform serum CrCl testing before initiating treatment with acamprosate (A3); if CrCl is between 30 and 50 mL/min or eGFR is between 30 and 59 mL/min/1.73 m^2, clinicians should adjust the dose according to the prescribing information or choose another medication. (A2)
- **Contraindications:** CrCl <30 mL/min or eGFR <30 mL/min/1.73 m^2

Oral or Injectable Long-Acting Extended-Release Naltrexone

- Because active alcohol use is not a contraindication to naltrexone therapy, clinicians should initiate naltrexone even if patients continue to use alcohol. (A1)
- 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 ensure that patients tolerate the medication. (A3)

☑ RECOMMENDATIONS

- Clinicians should recommend XR naltrexone if adherence to an oral regimen is a concern. (B3)
- **Contraindications:** Concomitant use of opioid analgesics or opioid agonists (e.g., methadone or buprenorphine), current physiologic opioid dependence, acute opioid withdrawal, reaction to a naloxone challenge test, or a positive urine test result for opioids
- For a patient with AUD who recently used opioids, the clinician should administer a naloxone challenge and confirm that the patient does not react, to ensure that opioids have been cleared from the system (see NYSDOH AI guideline Treatment of Opioid Use Disorder > Naltrexone). (A2)

Abbreviations: AUD, alcohol use disorder; CrCl, creatinine clearance; eGFR, estimated glomerular filtration rate; XR, extended-release.

Based on strong clinical evidence, acamprosate and oral or XR naltrexone are the preferred pharmacologic treatments for individuals with moderate or severe AUD who have a goal of reducing or abstaining from alcohol use [SAMHSA 2015; Jonas, et al. 2014]. 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 and meta-analyses have not consistently established the superiority of one medication over the other in reducing heavy drinking [Jonas, et al. 2014; Mann, et al. 2013; Anton, et al. 2006; Morley, et al. 2006; Kiefer, et al. 2003]. There is minimal and mixed evidence on whether combining naltrexone and acamprosate has an additive effect on alcohol consumption outcomes [Anton, et al. 2006; Kiefer, et al. 2003].

Acamprosate

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

In clinical trials comparing acamprosate treatment with 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 [Higuchi 2015; Plosker 2015; Gual and Lehert 2001; Tempesta, et al. 2000; Geerlings, et al. 1997; Pelc, et al. 1997; Poldrugo 1997; Sass, et al. 1996; Whitworth, et al. 1996; Paille, et al. 1995]. A meta-analysis from 2014 found that acamprosate was significantly associated with a decreased return to any drinking and with a decreased percentage of drinking days throughout treatment [Jonas, et al. 2014].

Who to treat: Acamprosate can be initiated if the individual is still actively using alcohol, but the efficacy of treatment during active alcohol use is unknown. Clinicians should initiate treatment with acamprosate as soon as the individual has abstained from alcohol use (within 7 days) for the best treatment response. Assessment of motivation will help identify candidates for acamprosate, which has been found to be most effective in patients with high levels of motivation [Jonas, et al. 2014]. Motivational interviewing (MI) may be used to enhance motivation.

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.

Initial and maintenance dosage: Oral acamprosate is typically started and continued as 3 doses daily, two 333 mg tablets for each dose for a total of 1,998 mg daily (see Table 1, below). Acamprosate may be maintained if the individual continues or returns to alcohol use.

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

Naltrexone

Efficacy: 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 [Ray, et al. 2010; Pettinati, et al. 2006; Mason, et al. 2002]. Naltrexone may also decrease subjective cravings for alcohol [Maisel, et al. 2013].

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 more effectively reduces alcohol consumption in individuals who use nicotine or cigarettes than those who do not [Anton, et al. 2018; Fucito, et al. 2012], which may be one factor in selecting pharmacologic treatment.

Who to treat: Active alcohol use is not a contraindication to initiating or maintaining treatment with naltrexone (oral and XR formulations). For some patients, reduced alcohol use rather than abstinence may be a treatment goal. If alcohol use is significantly reduced abruptly, individuals should be monitored for alcohol withdrawal syndrome.

Naltrexone is a preferred AUD treatment option in patients with aspartate aminotransferase/alanine aminotransferase levels within 3 to 5 times the upper limit of normal [Kwo, et al. 2017; Turncliff, et al. 2005], but it should be prescribed with caution in patients with abnormal liver function [FDA 2022; FDA 2013]. With follow-up liver tests and symptom monitoring, naltrexone has been used safely and effectively in people with liver disease, including compensated cirrhosis [Ayyala, et al. 2022]. In patients with abnormal liver function, baseline assessment of liver function should be performed before treatment initiation, and the extent of liver abnormalities may guide continued testing or referral to an experienced liver specialist. Clinicians can consider performing follow-up liver function tests 4 to 12 weeks after initiating naltrexone treatment [Lucey, et al. 2008].

Individuals with AUD should be abstinent from opioids for approximately 7 to 14 days before initiating XR naltrexone, which is also a U.S. Food and Drug Administration-approved treatment for opioid use disorder (see NYSDOH AI guideline Treatment of Opioid Use Disorder > Naltrexone). Clinicians should confirm the length of time since last opioid use by performing a naloxone challenge. Administer intranasal naloxone as available (e.g., 4 mg/0.1 mL) and observe the reaction. 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.

Oral naltrexone: The recommended induction and maintenance doses 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. Some clinicians advise patients to initiate naltrexone with a dose of 25 mg on day 1 and increase the dose to 50 mg on day 2. 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 [Srisurapanont and Jarusuraisin 2005; Chick, et al. 2000]. Because of oral naltrexone's short half-life, the timing of the daily dose should be considered. Advise patients taking oral naltrexone to monitor alcohol cravings and medication effectiveness throughout the day and adjust the timing of the naltrexone dose accordingly. For example, if a patient tends to experience cravings or use alcohol at night, taking naltrexone in the evening may be more effective than in the morning. Assessing and supporting a patient's ability to adhere to oral naltrexone before starting treatment (e.g., via MI) is essential. Engaging family members or others to assist with adherence to oral naltrexone can be helpful. XR naltrexone may improve adherence compared with oral naltrexone [Hartung, et al. 2014].

Injectable XR naltrexone: 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 ensure patients tolerate the medication. 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 patients with a prescription for daily oral naltrexone (50 mg daily) to take until they can receive the injection.

Adverse events: Oral and XR naltrexone are generally well tolerated. The more common adverse events include gastrointestinal symptoms (e.g., nausea, vomiting, abdominal pain, diarrhea) and dizziness [FDA 2022; FDA 2013]. Gastrointestinal adverse events associated with naltrexone may be more common among women than 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, which may be difficult in an individual with cachexia.

Table 1: Preferred Pharmacologic Treatment of Alcohol Use Disorder in Nonpregnant Adults [a]		
Medication [b]	**Dosage**	**Considerations**
Acamprosate oral (Campral)	**Initial and maintenance:** 666 mg 3 times per day	• Initiate treatment as soon as patients have abstained from alcohol use and within 7 days. • Counsel patients about the importance of adherence. • Perform serum CrCl testing before initiating treatment; adjust dose if CrCl is between 30 and 50 mL/min or eGFR is between 30 and 59 mL/min/1.73 m^2. • **Contraindications:** 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 effects occur, clinicians can consider a reduced dose of 25 mg once daily. • 100 mg daily has been used and well tolerated in studies.	• Abstinence from alcohol is not required for initiating and maintaining treatment. • Recommend the injectable formulation for patients who have problems with adherence to the oral regimen. • Abstinence from opioids is required for treatment. For patients who use alcohol and opioids, see recommendations in NYSDOH AI guideline Treatment of Opioid Use Disorder > Naltrexone. • Prescribe with caution in patients with abnormal liver function 3 to 5 times the upper limit of normal [FDA 2022; FDA 2013]. The extent of liver abnormalities on baseline testing may guide continued testing or referral to an experienced liver specialist. • **Contraindications:** Concomitant use of opioid analgesics or opioid agonists (e.g., methadone or buprenorphine), current physiologic opioid dependence, acute opioid withdrawal, reaction to a naloxone challenge test, or a positive urine test result for opioids
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	

Abbreviations: AUD, alcohol use disorder; CrCl, creatinine clearance; eGFR, estimated glomerular filtration rate; XR, extended-release.

Notes:

a. For treatment of pregnant individuals with AUD, see NYSDOH AI guideline Substance Use Disorder Treatment in Pregnant Adults > Alcohol Use and Alcohol Use Disorder Treatment During Pregnancy.
b. Consult package insert for full prescribing information for each medication.

Alternative Pharmacologic Treatment

☑ RECOMMENDATIONS

Alternative Pharmacologic Treatment

- For individuals with AUD who have not responded to or are intolerant of naltrexone or acamprosate, or who prefer a different medication, clinicians should discuss and offer disulfiram, gabapentin, or topiramate. (A3) See Table 2: Alternative Pharmacologic Treatment of Alcohol Use Disorder in Nonpregnant Adults.

Disulfiram

- Clinicians should emphasize the importance of avoiding alcohol consumption in all forms to patients before initiating and when taking disulfiram. (A3)
- Clinicians should perform liver function testing, including AST/ALT levels before initiating disulfiram. In patients with AST/ALT levels >3 to 5 times the upper limit of normal, avoid treatment with disulfiram. (A3)

☑ RECOMMENDATIONS

- **Contraindications:** Recent or concomitant use of metronidazole, alcohol, or alcohol-containing preparations (e.g., cough syrups, tonics). Disulfiram is contraindicated in the presence of severe myocardial disease or coronary occlusion and psychoses.

Gabapentin or Topiramate

- If gabapentin or topiramate is the agent of choice, clinicians should not require abstinence before initiation, because active alcohol use is not a contraindication to either medication. (A3)

Abbreviations: AUD, alcohol use disorder; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

For individuals with AUD who have not responded to or are intolerant of naltrexone or acamprosate, or who prefer a different medication, alternative treatment options include disulfiram, gabapentin, and topiramate (see Table 2, below). Of the 3 medications, only disulfiram is approved by the Food and Drug Administration (FDA) for AUD treatment. Other alternative treatments for AUD, including baclofen and varenicline, have been investigated, but the evidence of their efficacy is mixed [Agabio, et al. 2023; Bahji, et al. 2022; Fischler, et al. 2022]. Further studies are needed to confirm the benefits of these treatments for AUD.

Disulfiram

Efficacy: Concomitant use of alcohol and disulfiram can produce a severe physiologic response (the disulfiram-ethanol reaction) that may result in low blood pressure, tachycardia, facial flushing, nausea, vomiting, dyspnea, sweating, dizziness, blurred vision, and confusion [Bell and Smith 1949]. The psychological threat of the 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 reduction in alcohol consumption [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 effectively improved consumption outcomes in open-label trials (no blinding for participants or researchers) but not 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 [Brewer, et al. 2017; Skinner, et al. 2014; Jørgensen, et al. 2011; Fuller, et al. 1986].

Who to treat: Disulfiram is an alternative treatment option for individuals who have a clear goal of alcohol abstinence and are able to abstain for at least 12 hours before initiating treatment. Clinicians should advise patients that adverse effects may occur with alcohol consumption for up to 14 days after taking disulfiram.

Before initiating treatment with disulfiram, clinicians should perform baseline liver function testing, including AST/ALT tests, and consider disulfiram as an option only if AST/ALT levels are within 3 to 5 times the upper limit of normal [Kwo, et al. 2017]. Disulfiram has been associated with mild increases in hepatic enzymes in approximately 25% of individuals taking the medication [Björnsson, et al. 2006]. Acute and potentially fatal hepatotoxicity is very rare (1 per 10,000 to 30,000 years of disulfiram treatment) [Björnsson, et al. 2006]. It may be useful for clinicians to obtain follow-up liver test results within 1 month of initiating treatment. The extent of liver abnormalities should 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 2015].

Induction and maintenance dosage: The initial dose of disulfiram is 250 mg to 500 mg once daily for 1 to 2 weeks [FDA 2015]. After the initiation phase, the recommended maintenance dose of disulfiram is 125 mg to 500 mg once daily based on response and tolerability. Typically, the maintenance dose is 250 mg once daily; the maximum dose is 500 mg once daily (see Table 2, below).

Disulfiram does not reduce an individual's alcohol cravings. Motivation and consistent adherence are required for disulfiram to be an effective 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 [Johnson 2008; Laaksonen, et al. 2008; O'Farrell, et al. 1995; Chick, et al. 1992].

Box 2: Patient Education Points on Disulfiram

- Any consumption of alcohol while taking disulfiram can result in flushing, throbbing in the 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.
- Alcohol may be found in cough and cold medicines, mouthwashes, tonics, sauces, vinegar, and other food or skin products.
- Adverse reactions to alcohol ingestion may occur for up to 14 days after disulfiram is discontinued.
- In case of a severe adverse reaction, carry a wallet card or wear a medication bracelet advising emergency responders of disulfiram use.

Adverse events: Consuming alcohol while taking disulfiram can result in the adverse reactions described above. Because disulfiram is contraindicated in individuals with severe myocardial disease or coronary occlusion, 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 2015].

Gabapentin

Efficacy: Gabapentin's mechanism of action in treating AUD is not fully understood, but evidence suggests that it modulates and stabilizes central stress systems dysregulated by alcohol use cessation [Roberto, et al. 2010; Roberto, et al. 2008]. Although gabapentin is not approved by the FDA for AUD treatment, its use has been associated with reductions in alcohol consumption and craving [Mason, et al. 2018; Mason, et al. 2014]. As an adjunct to benzodiazepines, gabapentin is effective in treating common symptoms of acute and protracted alcohol withdrawal, including anxiety and sleep disturbances [Mason, et al. 2018; Rosenberg, et al. 2014; Lavigne, et al. 2012; Myrick, et al. 2009; Brower, et al. 2008; Bazil, et al. 2005; Karam-Hage and Brower 2000]. Gabapentin may be used to prevent alcohol withdrawal when indicated, e.g., for a hospitalized patient being treated for a condition not related to alcohol withdrawal [Maldonado 2017].

Box 3: Gabapentin Misuse

- 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, and there is the potential for misuse.
- Individuals may take gabapentin for recreational purposes, to control mood or anxiety, to intensify the effects of substances, or for intentional self-harm.
- Gabapentin has been increasingly associated with opioid-related overdose deaths, and caution is required when prescribing gabapentin for individuals with comorbid AUD and OUD [Kuehn 2022; Mattson, et al. 2022].
- If there is a strong concern about gabapentin misuse or diversion, clinicians may want to schedule more frequent follow-up visits and medication counts [Mersfelder and Nichols 2016; Smith, et al. 2016].

Who to treat: At doses of up to 1,800 mg daily, gabapentin is safe and well tolerated in individuals with AUD [Mason, et al. 2018; Mason, et al. 2014]. No adverse effects have been reported with concomitant use of gabapentin and alcohol, so alcohol abstinence is not required for gabapentin initiation [Myrick, et al. 2007]. Gabapentin is excreted through the kidneys; clinicians may consider testing 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.

Induction and maintenance dosage: The initial dose of gabapentin is 300 mg once daily, with increases in increments of 300 mg every 1 to 2 days based on improvement in symptoms 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), up to 2,400 mg or 3,600 mg per day, divided into 3 doses, can be considered for maintenance [FDA(b) 2017].

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

Topiramate

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

Like gabapentin, topiramate is not approved by the FDA for AUD treatment, but it has been associated with fewer drinking days, fewer drinks per drinking day, a decreased percentage of heavy drinking days, and an 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 preinitiation alcohol abstinence or detoxification [Maisel, et al. 2013].

Who to treat: Clinicians can offer topiramate as an alternative therapy to patients with moderate or 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 or maintaining treatment.

Induction and maintenance dosage: 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 [Knapp, et al. 2015; Kranzler, et al. 2014; Johnson, et al. 2003]. In patients with moderate-to-severe renal impairment, a 50% dose reduction is advised [Guerrini and Parmeggiani 2006; Perucca 1997].

Adverse effects: Adverse effects that occurred in more than 10% of study subjects include paresthesia [Swietach, et al. 2003; Spitzer, et al. 2002; Fujii, et al. 1993] 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 [Ma, et al. 2007; Cerminara, et al. 2006], acute visual disturbances, and myopia and acute angle-closure glaucoma [Shank and Maryanoff 2008].

Table 2: Alternative Pharmacologic Treatment of Alcohol Use Disorder in Nonpregnant Adults [a]

Medication [b]	**Dosage**	**Considerations**
Disulfiram oral (multiple brands)	**Initial and maintenance:** 500 mg once daily for 1 to 2 weeks. Reduce to 250 mg once daily.	• Abstinence from alcohol before initiating and while taking disulfiram is required. – Advise patients to initiate disulfiram only after 12 hours of abstinence. – Inform patients of the disulfiram-ethanol reaction [c]. – Reinforce complete abstinence from any form of alcohol. • 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. • **Contraindications:** Recent or concomitant use of metronidazole, alcohol, or alcohol-containing preparations (e.g., cough syrups, tonics). Disulfiram is contraindicated in the presence of severe myocardial disease or coronary occlusion and psychoses.
Gabapentin oral (multiple brands)	**Initial:** 300 mg once daily **Titrate:** Increase in increments of 300 mg. **Maintenance:** Up to 3,600 mg daily, divided into 3 doses; dose is based on response and tolerance.	• Abstinence from alcohol is not required for initiating or maintaining treatment. • **Caution:** Gabapentin may be misused alone for psychoactive effect or combined with opioids, benzodiazepines, alcohol, or other substances to intensify intoxication.

Table 2: Alternative Pharmacologic Treatment of Alcohol Use Disorder in Nonpregnant Adults [a]		
Medication [b]	**Dosage**	**Considerations**
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	• Abstinence from alcohol is not required for initiating or maintaining treatment. • 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.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; AUD, alcohol use disorder; CrCl, creatinine clearance; eGFR, estimated glomerular filtration rate.

Notes:

a. For treatment of pregnant individuals with AUD, see NYSDOH AI guideline Substance Use Disorder Treatment in Pregnant Adults > Alcohol Use and Alcohol Use Disorder Treatment During Pregnancy.
b. Consult package insert for full prescribing information for each medication.
c. Concomitant use of disulfiram and alcohol, even small amounts, can result in the following adverse effects: flushing, throbbing in the 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

Who to Treat

- Clinicians should recommend and offer pharmacologic treatment to individuals with moderate or severe AUD. (A1) See the guideline section Preferred Pharmacologic Treatment.
- Clinicians should recommend behavioral treatment for individuals with AUD and refer as appropriate. (A1) See the guideline section Behavioral Treatment.

Treatment Goals and Selection

- Clinicians should inform patients with AUD about all available pharmacologic and behavioral treatment options and all available treatment settings, including outpatient primary care and addiction specialty treatment (intensive outpatient, inpatient, and residential treatments). (A3)
- Clinicians should engage in shared decision-making with patients to set specific treatment goals, including harm reduction. (A3)
- Clinicians and patients should choose a pharmacologic agent based on evidence-based recommendations; patient preference; current level of alcohol use [a]; experience of cravings; risk of withdrawal syndrome; available support; available formulations; potential adverse effects; dosing schedules (adherence may be increased with once-daily dosing); medical or psychiatric comorbidities that may preclude use of a specific agent or require increased monitoring, including hepatic or renal dysfunction; depression or anxiety; a concomitant SUD; and concomitant opioid use or misuse. (A3)

Alcohol Withdrawal Syndrome

- Before initiating AUD treatment, clinicians should assess the need for withdrawal management. (A3) Mild-to-moderate withdrawal syndrome can be managed in the outpatient setting; severe withdrawal syndrome or other complicating conditions should be referred for inpatient management [b].

Follow-Up

- If a patient taking acamprosate or naltrexone for AUD continues or resumes alcohol use, the clinician should continue to prescribe the medication, advise the patient to continue treatment, and discuss possible modifications to treatment goals. (A3)

Behavioral Treatment

- Clinicians should recommend behavioral treatment for patients with AUD and refer as appropriate. (A1) The type of treatment is based on the individual patient's experience and preference, social factors, treatment availability, and insurance, among other factors.

Preferred Pharmacologic Treatment

- Clinicians should recommend oral acamprosate or oral or injectable XR naltrexone as the preferred medication for AUD treatment. (A1) See Table 1: Preferred Pharmacologic Treatment of Alcohol Use Disorder in Nonpregnant Adults.

Acamprosate

- For the best treatment response, clinicians should initiate treatment with acamprosate as soon as patients have abstained from alcohol use and within 7 days. (A3)
- Clinicians should perform serum CrCl testing before initiating treatment with acamprosate (A3); if CrCl is between 30 and 50 mL/min or eGFR is between 30 and 59 mL/min/1.73 m^2, clinicians should adjust the dose according to the prescribing information or choose another medication. (A2)
- **Contraindications:** CrCl <30 mL/min or eGFR <30 mL/min/1.73 m^2

Oral or Injectable Long-Acting Extended-Release Naltrexone

- Because active alcohol use is not a contraindication to naltrexone therapy, clinicians should initiate naltrexone even if patients continue to use alcohol. (A1)
- 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 ensure that patients tolerate the medication. (A3)
- Clinicians should recommend XR naltrexone if adherence to an oral regimen is a concern. (B3)

☑ ALL RECOMMENDATIONS: TREATMENT OF ALCOHOL USE DISORDER

- **Contraindications:** Concomitant use of opioid analgesics or opioid agonists (e.g., methadone or buprenorphine), current physiologic opioid dependence, acute opioid withdrawal, reaction to a naloxone challenge test, or a positive urine test result for opioids
- For a patient with AUD who recently used opioids, the clinician should administer a naloxone challenge and confirm that the patient does not react, to ensure that opioids have been cleared from the system (see NYSDOH AI guideline Treatment of Opioid Use Disorder > Naltrexone). (A2)

Alternative Pharmacologic Treatment

- For individuals with AUD who have not responded to or are intolerant of naltrexone or acamprosate, or who prefer a different medication, clinicians should discuss and offer disulfiram, gabapentin, or topiramate. (A3) See Table 2: Alternative Pharmacologic Treatment of Alcohol Use Disorder in Nonpregnant Adults.

Disulfiram

- Clinicians should emphasize the importance of avoiding alcohol consumption in all forms to patients before initiating and when taking disulfiram. (A3)
- Clinicians should perform liver function testing, including AST/ALT levels before initiating disulfiram. In patients with AST/ALT levels >3 to 5 times the upper limit of normal, avoid treatment with disulfiram. (A3)
- **Contraindications:** Recent or concomitant use of metronidazole, alcohol, or alcohol-containing preparations (e.g., cough syrups, tonics). Disulfiram is contraindicated in the presence of severe myocardial disease or coronary occlusion and psychoses.

Gabapentin or Topiramate

- If gabapentin or topiramate is the agent of choice, clinicians should not require abstinence before initiation, because active alcohol use is not a contraindication to either medication. (A3)

Abbreviations: AUD, alcohol use disorder; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CrCl, creatinine clearance; eGFR, estimated glomerular filtration rate; SUD, substance use disorder; XR, extended-release.

Notes:

a. Disulfiram is contraindicated in individuals who are actively using alcohol. See the guideline section Alternative Pharmacologic Treatment > Disulfiram.
b. See the American Society of Addiction Medicine (ASAM) Clinical Practice Guideline on Alcohol Withdrawal Management 2020.

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Supplement: Guideline Development and Recommendation Ratings

Table S1: Guideline Development: New York State Department of Health AIDS Institute Clinical Guidelines Program	
Developer	New York State Department of Health AIDS Institute (NYSDOH AI) Clinical Guidelines Program
Funding source	NYSDOH AI
Program manager	Clinical Guidelines Program, Johns Hopkins University School of Medicine, Division of Infectious Diseases. See Program Leadership and Staff.
Mission	To produce and disseminate evidence-based, state-of-the-art clinical practice guidelines that establish uniform standards of care for practitioners who provide prevention or treatment of HIV, viral hepatitis, other sexually transmitted infections, and substance use disorders for adults throughout New York State in the wide array of settings in which those services are delivered.
Expert committees	The NYSDOH AI Medical Director invites and appoints committees of clinical and public health experts from throughout New York State to ensure that the guidelines are practical, immediately applicable, and meet the needs of care providers and stakeholders in all major regions of New York State, all relevant clinical practice settings, key New York State agencies, and community service organizations.
Committee structure	• Leadership: AI-appointed chair, vice chair(s), chair emeritus, clinical specialist(s), JHU Guidelines Program Director, AI Medical Director, AI Clinical Consultant, AVAC community advisor • Contributing members • Guideline writing groups: Lead author, coauthors if applicable, and all committee leaders
Disclosure and management of conflicts of interest	• Annual disclosure of financial relationships with commercial entities for the 12 months prior and upcoming is required of all individuals who work with the guidelines program, and includes disclosure for partners or spouses and primary professional affiliation. • The NYSDOH AI assesses all reported financial relationships to determine the potential for undue influence on guideline recommendations and, when indicated, denies participation in the program or formulates a plan to manage potential conflicts. Disclosures are listed for each committee member.
Evidence collection and review	• Literature search and review strategy is defined by the guideline lead author based on the defined scope of a new guideline or update. • A comprehensive literature search and review is conducted for a new guideline or an extensive update using PubMed, other pertinent databases of peer-reviewed literature, and relevant conference abstracts to establish the evidence base for guideline recommendations. • A targeted search and review to identify recently published evidence is conducted for guidelines published within the previous 3 years. • Title, abstract, and article reviews are performed by the lead author. The JHU editorial team collates evidence and creates and maintains an evidence table for each guideline.
Recommendation development	• The lead author drafts recommendations to address the defined scope of the guideline based on available published data. • Writing group members review the draft recommendations and evidence and deliberate to revise, refine, and reach consensus on all recommendations. • When published data are not available, support for a recommendation may be based on the committee's expert opinion. • The writing group assigns a 2-part rating to each recommendation to indicate the strength of the recommendation and quality of the supporting evidence. The group reviews the evidence, deliberates, and may revise recommendations when required to reach consensus.

Table S1: Guideline Development: New York State Department of Health AIDS Institute Clinical Guidelines Program	
Review and approval process	• Following writing group approval, draft guidelines are reviewed by all contributors, program liaisons, and a volunteer reviewer from the AI Community Advisory Committee. • Recommendations must be approved by two-thirds of the full committee. If necessary to achieve consensus, the full committee is invited to deliberate, review the evidence, and revise recommendations. • Final approval by the committee chair and the NYSDOH AI Medical Director is required for publication.
External reviews	• External review of each guideline is invited at the developer's discretion. • External reviewers recognized for their experience and expertise review guidelines for accuracy, balance, clarity, and practicality and provide feedback.
Update process	• JHU editorial staff ensure that each guideline is reviewed and determined to be current upon the 3-year anniversary of publication; guidelines that provide clinical recommendations in rapidly changing areas of practice may be reviewed annually. Published literature is surveilled to identify new evidence that may prompt changes to existing recommendations or development of new recommendations. • If changes in the standard of care, newly published studies, new drug approval, new drug-related warning, or a public health emergency indicate the need for immediate change to published guidelines, committee leadership will make recommendations and immediate updates and will invite full committee review as indicated.

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