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Medication Treatment for Alcohol Use Disorder

INTRODUCTION

Current evidence shows that medications are underused in the treatment of alcohol use disorder, including alcohol abuse and dependence.* This is of concern because of the high prevalence of alcohol problems in the general population.[1,2] For example, data show that an estimated 10 percent to 20 percent of patients seen in primary care or hospital settings have a diagnosable alcohol use disorder.[3,4] People who engage in risky drinking often have physical and social problems related to their alcohol use. Problems with alcohol influence the incidence, course, and treatment of many other medical and psychiatric conditions.[2]

Yet, of the 18.0 million people who met the criteria for alcohol dependence or abuse in 2013, only a small subset (1.4 million) received any type of formal treatment (excluding mutual-help groups)—ranging from a single meeting with a counselor to participation in a specialized treatment program.[3]

Although many experts in addiction believe that patients with moderate or severe alcohol-related problems should be offered medication-assisted treatment (MAT) on a routine basis,[1] considerable resistance to the use of MAT persists. A diagnosis of alcohol use disorder continues to carry significant social exclusion, which affects both the individual who receives the diagnosis and the health care professionals to whom that individual may turn for care. In part, the social exclusion continues because of a lack of understanding of alcohol use disorder as a treatable medical disorder[2] even though, more than 50 years ago, the American Medical Association (AMA) affirmed that dependence on alcohol and other drugs is a medical disorder.[5] The AMA encouraged physicians and other clinicians, health care organizations, and policymakers to frame all their activities and decisions in ways that reflect that fact.

Within this document "alcohol abuse" and "alcohol dependence" are used when discussing medication indications or research that is based upon this terminology. For a summary of important differences between DSM-IV and DSM-5, please see the box on this page.

Alcohol Use Disorder: A Comparison Between DSM-IV and DSM-5

"In May 2013, the American Psychiatric Association issued the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). Although there is considerable overlap between DSM-5 and DSM-IV, the prior edition, there are several important differences: DSM–IV described two distinct disorders, alcohol abuse and alcohol dependence, with specific criteria for each. DSM-5 integrates the two DSM-IV disorders, alcohol abuse and alcohol dependence, into a single disorder called alcohol use disorder (AUD) with mild, moderate, and severe subclassifications. Under DSM-5, anyone meeting any two of the 11 criteria during the same 12-month period would receive a diagnosis of AUD. The severity of an AUD—mild, moderate, or severe—is based on the number of criteria met:

- **Mild:** The presence of 2 to 3 symptoms
- **Moderate:** The presence of 4 to 5 symptoms
- **Severe:** The presence of 6 or more symptoms

The DSM-5 eliminates legal problems as a criterion, adds craving as a criterion for an AUD diagnosis and modifies some of the criteria descriptions with updated language."

—National Institute on Alcohol Abuse and Alcoholism[6]

To clarify the situation, the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and the Substance Abuse and Mental Health Services Administration (SAMHSA) jointly convened a Consensus Panel on New and Emerging Pharmacotherapies for Alcohol Use Disorders and Related Comorbidities (see Appendix A). The panel, which brought together experts in alcohol research, clinical care, medical education, and public policy, reviewed current evidence on the effectiveness of available medications for the treatment of alcohol use disorders and developed guidance for the use of medications in clinical practice.[1] The panel's guidance is summarized in this document.

CONSIDERING MEDICATIONS

Direct involvement of physicians and other health care professionals in identifying and treating alcohol use disorder is possible, practical, and necessary. The medications described here have been shown to be effective in, and are approved by the Food and Drug Administration (FDA) for, the management of alcohol dependence or the prevention of relapse to alcohol use.[7,8,9,10,11] Specifically:

- **Acamprosate calcium** is indicated for the maintenance of abstinence from alcohol in patients dependent on alcohol who are abstinent at treatment initiation.
- **Disulfiram** is an aid in the management of selected patients who want to remain in a state of enforced sobriety so that supportive and psychotherapeutic treatment may be applied to best advantage.
- **Oral naltrexone** (naltrexone hydrochloride tablet) is indicated for the treatment of alcohol dependence.
- **Extended-release injectable naltrexone** is indicated for the treatment of alcohol dependence in patients who have been able to abstain from alcohol in an outpatient setting.

Clinicians should consider prescribing one of these medications when treating a patient who is dependent on alcohol or who has stopped drinking but is experiencing problems including cravings or relapses. Patients with moderate or severe alcohol use disorder, including those who have physiologic dependence or who are experiencing cravings and have not improved in response to psychosocial approaches alone, are particularly strong candidates for medication-assisted treatment.[1,2]

Medications should be prescribed as part of a comprehensive treatment approach that includes counseling and other psychosocial therapies (through referral to a psychiatrist, psychologist, or professional counselor) and social supports (through participation in Alcoholics Anonymous and other mutual-help programs).[1,2]

Table 1 summarizes information about each medication approved by the FDA for the treatment of alcohol use disorder and/or the prevention of relapse to alcohol use.

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TABLE 1: Medications Approved for Use in the Treatment of Alcohol Use Disorder[†]

	Disulfiram	Naltrexone oral and extended release injectable formulations	Acamprosate delayed-release tablets
Frequency of Administration	Daily	Daily (oral) or monthly (extended-release injectable)	Three times per day
Principal Action	**When** taken in combination with alcohol, causes a significant physical reaction, involving nausea/vomiting, flushing, and heart palpitations. The knowledge that such reactions are likely if alcohol is consumed acts as a deterrent to drinking. **Given** sufficient amounts of alcohol in the patient's system, more severe reactions may occur, such as respiratory depression, cardiovascular collapse, arrhythmias, myocardial infarction, acute congestive heart failure, unconsciousness, convulsions, and death.	**Blocks** opiate receptors that are involved in the rewarding effects of drinking and craving for alcohol. **Extended-release** injectable naltrexone is administered every 4 weeks, thereby minimizing opportunities for nonadherence, as compared with daily oral ingestion. The monthly injection also produces a more consistent and predictable blood level of the drug, because the depot injection bypasses first-pass metabolism.	**Is** thought to reduce symptoms of protracted abstinence by counteracting the imbalance between the glutamatergic and GABAergic systems associated with chronic alcohol exposure and alcohol withdrawal.
Clinical Uses/Ideal Candidates	**Candidates** include patients dependent on alcohol who have completed alcohol withdrawal. Ideally, candidates are committed to abstinence and willing to take disulfiram under the supervision of a family member or treatment program.	**Oral** naltrexone and extended-release injectable naltrexone are indicated for the treatment of alcohol dependence in patients who can abstain from alcohol in an outpatient setting before the initiation of treatment. Naltrexone has not been shown to be effective in patients who are drinking at treatment initiation. **Both** formulations may have the greatest benefit in patients who can discontinue drinking on their own for several days before treatment initiation. **Extended-release** injectable naltrexone is also indicated for the prevention of relapse to opioid dependence following detoxification.	**Acamprosate** is indicated for the maintenance of abstinence in patients who are dependent on alcohol and are abstinent at treatment initiation. **The** efficacy of acamprosate in promoting abstinence has not been demonstrated in subjects who have not completed detoxification or who have not achieved alcohol abstinence before beginning treatment.

[†] This table highlights some properties of each medication. It does not provide complete information and is not intended as a substitute for the package inserts or other drug reference sources used by clinicians (see http://www.dailymed.nlm.nih.gov for current package inserts). For patient information about these and other drugs, visit the National Library of Medicine's MedlinePlus (http://www.medlineplus.gov). Whether a medication should be prescribed and in what amount are matters to be discussed between an individual and his or her health care provider. The prescribing information provided here is not a substitute for the clinician's judgment, and the National Institutes of Health and SAMHSA accept no liability or responsibility for use of the information in the care of individual patients.

	Disulfiram	Naltrexone oral and extended release injectable formulations	Acamprosate delayed-release tablets
Contraindications	**Contraindicated** in the presence of severe myocardial disease or coronary occlusion, psychoses, pregnancy, and in those with high levels of impulsivity, suicidality, and hypersensitivity to disulfiram or to other thiuram derivatives used in pesticides and rubber vulcanization. **Patients** who are taking or have recently taken metronidazole, paraldehyde, alcohol, or alcohol-containing preparations (e.g., cough syrups, tonics) should not be given disulfiram. **Disulfiram** labeling also includes several important precautions regarding drug–drug interactions. See the package insert for specific contraindications.	**Contraindicated** in patients receiving opioid analgesics and those receiving long-term opioid therapy or anticipating a need for opioids (e.g., surgery), because it could precipitate a severe opioid withdrawal or block opioid analgesia; patients currently dependent on opioids, including those being maintained on opioid agonists such as methadone or partial agonists such as buprenorphine; patients in acute opioid withdrawal; patients who have failed the naloxone challenge test or whose urine tests positive for opioids. **Contraindicated** in patients with a history of sensitivity to polylactide-co-glycolide, carboxymethyl cellulose, or any components of the diluent used for the injectable medication. **It** should not be given to patients whose body mass precludes intramuscular (IM) injection with the 2-inch needle provided. Inadvertent subcutaneous injection may cause a severe injection-site reaction. **Although** not in current labeling, the consensus of the panel is that use should be avoided in patients with serum aminotransferase levels greater than five times the upper limit of normal, except where the benefits outweigh the risks.	**Contraindicated** in patients with severe renal impairment and in those who have a known hypersensitivity to the drug or its components.

	Disulfiram	Naltrexone oral and extended release injectable formulations	Acamprosate delayed-release tablets
Warnings	**Use** with caution in patients with heart disease, diabetes, hypothyroidism, epilepsy, cerebral damage, chronic or acute nephritis, acute hepatitis or other hepatic diseases, and in patients older than 60. **Hepatic** toxicity (including hepatic failure resulting in liver transplantation or death) has been infrequently reported. Severe and sometimes fatal hepatitis associated with disulfiram may develop after many months of therapy. Hepatic toxicity has occurred in patients with or without a history of abnormal liver function. **Patients** should be advised to immediately notify their physician of any early symptoms of hepatitis, including fatigue, weakness, malaise, anorexia, nausea, vomiting, jaundice, or dark urine. **Liver** function tests (taken at baseline and 10–14 days later) are suggested to detect any hepatic dysfunction that may result from disulfiram therapy. In addition, complete blood counts and serum chemistries, including liver function tests, should be monitored. **Psychotic** reactions have been noted, attributable to the unmasking of underlying psychoses in patients.	**Cases** of hepatitis and clinically significant liver dysfunction were observed in association with extended-release injectable naltrexone treatment. Discontinue use of naltrexone in the event of symptoms or signs of acute hepatitis. **Use** with caution in patients with moderate to severe renal impairment. **Patients** should take no opioids, including opioid-containing medications, for a minimum of 7 days before starting naltrexone to avoid precipitating opioid withdrawal. **Patients** needing opioid analgesia or patients with a history of opioid use disorder may respond to lower doses of opioids after treatment with extended-release injectable naltrexone. Failure to carefully titrate opioid dose could result in potentially life-threatening opioid intoxication and overdose. **Patients** should be told of the serious consequences of trying to overcome the opioid blockade.	**Before** initiating treatment with acamprosate, evaluate the patient's renal function through a standard panel for urea, electrolytes, and serum creatinine to rule out severe renal impairment. **For** patients with moderate renal impairment (creatinine clearance of 30–50 mL/min), a reduced dose of acamprosate (one 333 mg tablet 3 times a day) is recommended. **Because** of elevated risk of diminished renal function in people ages 65 or older, baseline and frequent renal function tests are important in this population.

	Disulfiram	Naltrexone oral and extended release injectable formulations	Acamprosate delayed-release tablets
Use in Pregnant and Postpartum Women	***Pregnancy:*** The FDA has not assigned a pregnancy category. The safe use of this drug in pregnancy has not been established. Therefore, disulfiram should be used during pregnancy only when, in the judgment of the physician, the probable benefits outweigh the possible risks. ***Nursing:*** Do not give disulfiram to nursing mothers.	***Pregnancy:*** FDA Pregnancy Category C‡ ***Nursing:*** Transfer of naltrexone and 6ß-naltrexol into human milk has been reported with oral naltrexone. Because animal studies have shown that naltrexone has a potential for tumorigenicity and other serious adverse reactions in nursing infants, an individualized treatment decision should be made whether a nursing mother will need to discontinue breastfeeding or discontinue naltrexone.	***Pregnancy:*** FDA Pregnancy Category C‡ ***Nursing:*** It is not known whether acamprosate is excreted in human milk.

SOURCE: SAMHSA and NIAAA. (2012, September). *Report of the SAMHSA-NIAAA Consensus Panel on New and Emerging Pharmacotherapies for Alcohol Use Disorders and Related Comorbidities.* Rockville, MD: SAMHSA.

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‡ Animal studies have shown an adverse effect on the fetus and there are no adequate, well-controlled studies in humans, but potential benefits may warrant use of the drug in some pregnant women despite potential risks.

As a result, the following factors need to be considered when prescribing pharmacotherapy to older adults:[45,46]

- Dose reductions and frequent renal function tests may be necessary when prescribing acamprosate to individuals in whom decreased renal function (creatinine clearance rate <70 mL/min/1.73 m^2) is evident.
- In patients ages 61 and older, disulfiram doses may need to be reduced. Disulfiram interacts with multiple drugs, so caution should be exercised in prescribing it to older adults at risk for polypharmacy.

Selecting a Medication

The FDA has approved three oral medications (disulfiram, acamprosate, and naltrexone) and one injectable medication (extended-release injectable naltrexone) for the treatment of alcohol dependence or the prevention of relapse to alcohol use.[7,24] In addition to factors specific to each medication, the clinician should consider the patient's past experience with particular medication-assisted treatment medications; beliefs and opinions about which pharmacotherapy may be most helpful; level of motivation for abstinence; medical status and contraindications for each medication; and history of medication adherence.[2]

Although further research with large patient samples is required before definitive advice can be offered on which medication to select for a particular patient, information for matching patients to particular pharmacotherapies is summarized below.[24,40,47,48,49] Medications are listed in the approximate order in which the FDA approved them for the treatment of alcohol dependence.

The FDA has approved three oral medications and one injectable medication for treatment of alcohol dependence or prevention of relapse to alcohol use.

Disulfiram. Approved by the FDA as an alcohol abuse deterrent in 1951, disulfiram disrupts the metabolism of alcohol, resulting in an unpleasant reaction, which can be severe whenever an individual taking disulfiram consumes alcohol.[50,51,52,53,54]

Mechanism of Action. The disulfiram reaction is caused by a blockade of aldehyde dehydrogenase, which causes an accumulation of acetaldehyde when alcohol is ingested. When this occurs, the physical reaction can include nausea, flushing, and heart palpitations.[40] Unlike other medications approved to treat alcohol use disorder, disulfiram does not directly affect opiate, gaba-aminobutyric acid, or glutamate receptors in the brain. Disulfiram blocks dopamine-beta-hydroxylase in the brain, thereby increasing dopamine levels and reducing noradrenaline levels.[51]

Formulation. Disulfiram is manufactured as a white to off-white odorless and almost tasteless powder. It is supplied in 250 mg and 500 mg tablets for oral administration.[50]

Dosing and Administration. The initial and average maintenance dose is 250 mg per day (doses range from 125 mg to a maximum dose of 500 mg per day). The disulfiram tablet is taken by mouth once a day; it may be crushed and mixed with water, coffee, tea, milk, soft drink, or fruit juice.[50] Faulty bioactivation in some patients can yield too low a concentration of the active metabolite needed to inhibit aldehyde dehydrogenase, and the 500 mg dose may be more effective in these patients.[52] Patients who experience mild side effects (as described later in this section) may obtain relief by reducing the dose to 125 mg daily.[51]

Efficacy. The effectiveness of disulfiram in the prevention and limitation of relapse to alcohol use is supported by multiple studies.[47,48] It should be noted that disulfiram was approved prior to the requirement that drugs be shown to be effective before being marketed was enacted. An evidence report from the Agency for Healthcare Research and Quality concluded that four placebo-controlled randomized clinical trials of oral disulfiram produced mixed results.[49] Although disulfiram was shown to reduce the frequency of drinking days in two trials, in neither study did it improve relapse rates compared with placebo. Two studies that examined patient adherence with oral disulfiram found it to be low,[53,54] and a third study had a 46 percent dropout rate.[55]

Investigators who argue that disulfiram is effective in preventing relapse to alcohol use frequently emphasize the importance of the

circumstances in which it is administered. In particular, the level and quality of supervision a patient receives while taking disulfiram are believed to be important components of its success.[55,56] Some studies have found that court-ordered disulfiram therapy promotes efficacy by increasing adherence to the disulfiram regimen.[57] Use of incentives, patient contracts, the cooperation of a significant other in fostering adherence, the use of regular reminders to the patient, and patient behavioral counseling and social support may enhance disulfiram efficacy by improving adherence. Overall, methodologic limitations and mixed results make it difficult to state with certainty what percentage of patients benefit from disulfiram.[1] However, disulfiram is a medication that should be considered for patients with no contraindications and who might have major consequences should they use alcohol.

Safety. The severity of a disulfiram–alcohol interaction is proportional to the dose of disulfiram and the amount of alcohol consumed. A reaction lasts 30 to 60 minutes in mild cases. In more severe cases, the reaction can continue for several hours or until the alcohol is metabolized. When effects are severe, palliative and supportive measures may be needed to restore blood pressure and treat shock.[50]

Other safety issues include both minor side effects and more serious adverse reactions. Minor side effects, which typically occur during the first 2 weeks of therapy, include skin/acneiform eruptions, headache, allergic dermatitis, impotence, mild drowsiness, fatigue, and metallic or garlic-like aftertaste.[2,50]

Serious adverse reactions, although rare,[51] include the following conditions:[2,50]

- *Optic neuritis:* Usually diagnosed after a patient complains of visual disturbances, optic neuritis is addressed by discontinuing disulfiram and conducting (or referring the patient for) an ophthalmologic examination.
- *Peripheral neuritis, polyneuritis, peripheral neuropathy:* Usually diagnosed after a patient complains of paresthesias (numbness or tingling), these conditions require that disulfiram be discontinued. A neurological evaluation should be conducted.
- *Hepatitis, including cholestatic and fulminant hepatitis, as well as hepatic failure:* When symptoms of hepatic dysfunction are reported or observed, liver function tests should be obtained. When clinical or laboratory evidence of hepatic dysfunction is found, disulfiram should be discontinued immediately and liver function and other symptoms monitored closely.

Drug Interactions. There is evidence that disulfiram interacts with a number of drugs, including benzodiazepines, isoniazid, rifadin (Rifampin®), metronidazole, oral anticoagulants such as warfarin, oral hypoglycemics, phenytoin, and theophylline. The potential severity of some drug interactions makes it essential that patients be cautioned to report all medications they are taking and not to start any new medication without checking with the disulfiram prescriber.[14,53]

Clinical Recommendations. Patients who are good candidates for treatment with disulfiram include those who are motivated for treatment and want to achieve abstinence, who are medically appropriate, who can receive supervised dosing, and who understand the consequences of drinking alcohol while taking disulfiram. It may be an appropriate short-term therapy for a patient in recovery who anticipates being in a situation that may trigger craving for alcohol (e.g., a family holiday visit) and who requests an additional incentive to remain abstinent.[2,53,54,55,56,57]

Naltrexone. Naltrexone hydrochloride is a long-acting opioid antagonist. The FDA approved oral naltrexone for the treatment of alcohol dependence or alcoholism in 1994. The low rate of retention and adherence encountered with oral naltrexone led to the development of the extended-release injectable formulation, which the FDA approved for the treatment of alcohol use disorder in 2006.[2,24]

The actual neurobiological mechanisms by which naltrexone induces the reduction in alcohol consumption observed in alcohol-dependent patients is not entirely understood. Preclinical data suggest the involvement of the endogenous opioid system.

Mechanism of Action. Naltrexone has affinity for the mu, kappa, and delta opiate receptors. The actual neurobiological mechanisms by which

naltrexone induces the reduction in alcohol consumption observed in alcohol-dependent patients is not entirely understood. Preclinical data suggest the involvement of the endogenous opioid system.[58]

As an antagonist at the mu receptor, naltrexone may reduce the urge to consume alcohol through two mechanisms:

1. Suppression of alcohol-mediated beta-endorphin stimulation of dopamine neurons in the nucleus accumbens
2. Reduction of beta-endorphin disinhibition of the tonic inhibition of dopamine cells by gamma-aminobutyric acid neurons in the ventral tegmental area[47,59,60]

Extended-release injectable naltrexone is metabolized in the liver to the opioid antagonist 6ß-naltrexol.[61] Two peak blood levels occur after injection: a transient initial peak occurs approximately 2 hours after injection and a second peak occurs approximately 2 days later. About 14 days after injection, the blood level slowly begins to decline in a linear fashion. The absorption of extended-release naltrexone is mediated by its gradual and prolonged release for 2 to 4 weeks after injection through hydrolysis of copolymer microspheres.[7,24]

Formulation. Oral naltrexone is marketed in 50 mg tablets.[7,24]

Extended-release injectable naltrexone was developed by embedding the drug molecule within microspheres composed of a biodegradable copolymer, resulting in release of the active ingredient over a period of approximately 4 weeks.[62,63] It is packaged in a kit containing a vial of naltrexone as a dry powder, which must be suspended in a liquid diluent immediately before use. Each kit contains a syringe and five needles: one for mixing the microspheres with the diluent and four needles (two 1.5-inch needles and two 2-inch needles) for injecting the suspension into the upper outer quadrant of the gluteal muscle.[63]

Kits must be refrigerated during storage but should be brought to room temperature approximately 45 minutes before an injection is given. The suspended microspheres in solution must be mixed vigorously to prevent clumping, which can clog the needle during injection.[63]

Dosing and Administration. The oral naltrexone tablet is taken by mouth once a day. The dose recommended for most patients is 50 mg per day, given in a single dose.[2,7] GI side effects are common and dose dependent, so patients with GI side effects should have a trial of therapy at a lower dose.

The approved dose of extended-release naltrexone is 380 mg, given approximately once a month. Clinical trial data confirm earlier studies indicating that there is no need to adjust the dose for the patient's body weight.[63]

Extended-release injectable naltrexone is administered by intramuscular (IM) gluteal injection. It is retained at the site of injection so that its active compound is released consistently over approximately 4 weeks,[63] and measurable levels may be observed for longer than 1 month.

Efficacy. Oral naltrexone has been shown to reduce relapse to heavy drinking, which is defined as three or more drinks per day for women and four or more for men.[59,60,64] In a systematic review of 11 double-blind, placebo-controlled trials, researchers found that oral naltrexone, when combined with psychosocial treatments, reduced relapse rates at 3 months in patients with alcohol dependence.[59] (Almost all studies were done in patients who were abstinent at baseline.) Short-term outcomes in favor of naltrexone included fewer patients relapsing to alcohol dependence (38% with naltrexone versus 60% with placebo), fewer patients returning to drinking (61% versus 69%), reduced craving for alcohol, and fewer drinking days. Thus, it is especially useful in patients who have a history of drinking relapses.[65]

Extended-release injectable naltrexone is approved for use only in patients who can refrain from drinking for several days before treatment begins—a subgroup of the patient population in whom efficacy has been demonstrated. For example, in a 6-month, randomized, double-blind, placebo-controlled trial involving 624 individuals, patients who received a 380 mg dose of extended-release injectable naltrexone had a 25 percent reduction in heavy drinking days compared with those receiving placebo. The effect was greater in males.[66] A secondary analysis found that patients who had 4 or more days of abstinence before beginning treatment with extended-release injectable naltrexone

experienced particularly good treatment outcomes.[67]

A side effect unique to extended-release injectable naltrexone is injection-site reaction, which involves pain or tenderness at the injection site.

Safety. Naltrexone generally is well tolerated, although it has the potential to precipitate severe opioid withdrawal in patients who are opioid dependent.[2] Common side effects include nausea, vomiting, headaches, dizziness, fatigue, anxiety, and somnolence, with nausea and vomiting the most frequently reported.[59,60,64,65,66,67,68] Less common side effects include diarrhea, constipation, chest pains, joint/muscle pain, rash, insomnia, excessive thirst, loss of appetite, perspiration, mild depression, increased tears, and delayed ejaculation.[2,24]

More serious adverse reactions, with suggestions for management, include the following:[59,60]

- *Precipitated opioid withdrawal:* To mitigate withdrawal symptoms, discontinue naltrexone, provide supportive treatments (i.e., hydration and antispasmodic and antidiarrheal medications) until the symptoms resolve, and provide a ß2-agonist such as clonidine. Watch for clonidine side effects, including dizziness, hypotension, fatigue, and headache.
- *Hepatic toxicity:* Discontinue naltrexone.
- *Naltrexone overdose:* Treat the patient symptomatically under close supervision. Contact a poison control center for current information.

A side effect unique to extended-release injectable naltrexone is injection-site reaction, which involves pain or tenderness at the injection site, usually resolving in 2 to 5 days. Swelling, erythema, bruising, and pruritus may occur, generally as the result of an inadvertent subcutaneous injection. Serious reactions include induration, cellulitis, hematoma, abscess, sterile abscess, and necrosis. Rarely, these reactions require surgical intervention, such as debridement of necrotic tissue, which can result in significant scarring. To prevent problems, providers should be trained in proper techniques for IM injections.[63]

Drug Interactions. Potential drug interactions involve cough and cold preparations, antidiarrheal medications, thioridazine, yohimbine, and nonsteroidal anti-inflammatory drugs (which can elevate liver enzymes).

As noted earlier, naltrexone blocks the effects of opioid analgesics.[13] For more information, see the discussion of Special Considerations in Pain Management on page 18.[13,14,68,69]

Clinical Recommendations: Oral Naltrexone. Oral naltrexone is most effective when prescribed for patients who are highly motivated and/or supported with observed daily dosing and who are abstinent at the time treatment is initiated.[70,71] Naltrexone also appears to be effective in the following patient populations:

- Patients who have a history of opioid use disorder and who are seeking treatment for an alcohol use disorder. Naltrexone reduces the reinforcing effects of and curbs cravings for both opioids and alcohol.
- Patients with intense craving for alcohol during treatment. These individual may experience greater medication benefit than patients with low levels of craving for alcohol.[72]
- Patients who have a family history of alcohol use disorder. Both laboratory studies and clinical trials suggest that patients with a family history of alcohol problems may benefit more from treatment with naltrexone than patients who do not have such a history.[73]

Clinical Recommendations: Extended-Release Injectable Naltrexone. Extended-release injectable naltrexone benefits people appropriate for treatment with oral naltrexone, as well as the following:[1,68,69,74]

- Patients who are abstinent at initiation of treatment. Extended-release injectable naltrexone has not been shown to be effective in patients who are drinking at the time treatment is initiated.
- Patients who are seeking treatment for moderate or severe alcohol use disorder while in recovery from co-occurring opioid use disorder. The FDA approved extended-release injectable naltrexone in 2010 for the

prevention of relapse to opioid dependence, following opioid detoxification.

Acamprosate. Acamprosate is a delayed-release synthetic compound that is indicated for maintaining abstinence in patients who are alcohol dependent and are abstinent at the time treatment is initiated.[75] The FDA approved the medication for the treatment of alcohol use disorder in 2004.[7]

Mechanisms of Action. Although the precise mechanisms of action of acamprosate are not yet known, they appear to involve beneficial modulation of the glutamatergic neurotransmitter system (including antagonism of the mGlu5 metabotropic glutamate receptor) to counteract the imbalance between the glutamatergic and GABAergic systems associated with chronic alcohol exposure and alcohol withdrawal.[75]

Formulation. Acamprosate is supplied as enteric-coated 333 mg tablets.[7]

Dosing and Administration. Two 333 mg delayed-release tablets are taken by mouth three times a day, with or without food (a lower dose may be effective with some patients and must be used with those with impaired renal function). Pills must be swallowed whole, not crushed or broken.[7,76]

Efficacy. Acamprosate has been shown to be an effective treatment for dependence on alcohol, with no abuse potential and no significant interaction with medications commonly used to treat substance use and mental disorders.[76] Acamprosate's efficacy is primarily due to its ability to reduce the negative symptoms associated with the period immediately following alcohol withdrawal.[77]

Safety. Acamprosate has a good safety profile: no development of tolerance has been reported, there appears to be no risk of overdose, and there is no clinically significant interaction between acamprosate and other medications. The most common side effect is diarrhea, which usually is mild and transient, typically disappearing within the first few weeks of treatment.[78] Less common side effects include intestinal cramps and flatulence, headache, increased or decreased libido, insomnia, anxiety, muscle weakness, and dizziness.

Rare but serious side effects include suicidal ideation and suicide attempts. In such patients, acamprosate should be discontinued and the patient monitored for worsening of depression.[76] A psychiatric consultation should be obtained and/or an antidepressant medication prescribed as needed.

Drug Interactions. There are no known drug interactions with acamprosate.[14,24]

Clinical Recommendations. Research on patient characteristics has not definitively identified particular characteristics that would predict which patients would benefit most from acamprosate.[77] However, evidence suggests that acamprosate may be most effective for the following types of patients:[59,79]

- Patients who are abstinent from alcohol at the time treatment is initiated and who are motivated to maintain abstinence. A study found that these patients had better outcomes with acamprosate than did patients who wanted only to reduce their drinking.[78]
- Patients with hepatic disease or those who are being treated with opioids for pain or addiction. Acamprosate is eliminated renally and does not affect endogenous or exogenous opioids.
- Patients who are coping with multiple medical issues and who are taking many other medications. There are no clinically significant drug interactions with acamprosate, so it can be a safe medication for many patients taking other medications.

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MEDICATION-ASSISTED TREATMENT

A patient who is being considered for medication-assisted treatment must be free of the contraindications listed in Table 1, including severe medical or psychiatric problems that would make the individual a poor candidate for treatment with a medication.[1,2]

The following steps are recommended for initiating treatment with any of the medications approved for the management of moderate or severe alcohol use disorder or the prevention of relapse to alcohol use:[1,2,7]

- Educate the patient about medication-assisted treatment and the specific medication being recommended.
- Obtain informed consent for medication-assisted treatment.
- Complete a medical, psychiatric, and substance use history, including history of cardiovascular disease, diabetes, thyroid disease, seizure disorder, central nervous system impairment, and kidney or liver disease.
- Determine which prescription and over-the-counter medications the patient is taking, including herbal preparations.
- Perform a physical examination, baseline liver and kidney function tests, urine toxicology screen, and (in women) a pregnancy test.
- Assess the patient for allergies to the proposed medication and to other medications.
- For women, assess reproductive status, including current pregnancy or plans to become pregnant or to breastfeed.

Initiating Treatment with Disulfiram

Steps in initiating treatment with disulfiram are as follows:[2,55,56]

- Wait until the patient has abstained from alcohol for at least 12 hours and/or until the breath or blood alcohol level is zero.
- Perform an electrocardiogram if clinically indicated (e.g., in a patient with a history of heart disease).
- Confirm the absence of allergy to disulfiram.
- Perform the following tests to confirm abstinence and determine baselines after stabilization:
  a. Breath or blood alcohol tests, if clinically indicated to confirm abstinence
  b. Liver function tests: alanine aminotransferase, aspartate aminotransferase, gamma glutamyl-transferase, alkaline phosphatase, lactate dehydrogenase, bilirubin, total protein, albumin, prothrombin time
  c. Complete blood count and routine chemistries, if clinically indicated
  d. Kidney function tests: routine blood urea nitrogen, creatinine

Initiating Treatment with Naltrexone

Naltrexone has not been shown to be effective in patients who are drinking at treatment initiation.

The clinician should consider how best to induct a prospective patient into treatment with extended-release injectable naltrexone.

Advise all patients being treated for alcohol use disorder that it is imperative to notify health care providers of any recent use of opioids or any history of opioid use disorder before starting extended-release injectable naltrexone, to avoid precipitation of opioid withdrawal. A urine drug screen should be conducted to verify abstinence before beginning induction.[80] If patients are to be treated for both alcohol and opioid substance use disorder, they should be off all opioids, including prescription opioid analgesics, for a minimum of 7 to 10 days before starting naltrexone.[81] Patients transitioning from opioid agonist therapy to extended-release injectable naltrexone may be vulnerable to precipitation of withdrawal symptoms for as long as 2 weeks. Ensure that patients understand that withdrawal precipitated by administration of an opioid antagonist is different from the experience of spontaneous withdrawal that occurs with discontinuation of opioids in a dependent individual. Withdrawal precipitated by an opioid antagonist may be severe enough to require hospitalization.

When discontinuing naltrexone for patients with a history of co-occurring opioid use disorder, advice on opioid overdose prevention should be provided. After a period of abstinence from opioids, tolerance is greatly reduced. This means a previously tolerated amount of opioid could result in opioid overdose. Patients discontinuing opioid antagonist therapy in order to receive pain management with opioid analgesics should also be advised of this risk. Consider providing patients at risk of opioid overdose with a prescription for naloxone. SAMHSA's *Opioid Overdose Toolkit* includes strategies for developing such a plan to address emergency reversal of actual or suspected opioid overdose.[82]

Pretreatment with oral naltrexone is not required before induction onto extended-release injectable naltrexone.[63,68]

Dosing and Administration. For appropriate candidates, the recommended dose of extended-release injectable naltrexone is 380 mg, delivered intramuscularly approximately every 30 days, alternating buttocks for each subsequent injection. The following cautions should be observed:[24,63,68]

- Injectable naltrexone should be administered only by a medical professional (a physician, nurse, physician assistant or nurse practitioner) who knows how to administer IM gluteal injections.
- Injectable naltrexone is packaged in a kit containing a vial of naltrexone as a dry powder that must be reconstituted with a liquid diluent immediately before use. Kits must be refrigerated during storage but should be brought to room temperature approximately 45 minutes before an injection is given. The reconstituted microspheres in solution must be mixed vigorously to prevent clumping, which can clog the needle during injection.
- A syringe and five needles are provided: one for mixing the microspheres with the diluent and four needles (two 1.5-inch needles and two 2-inch needles) for injecting the suspension into the upper outer quadrant of the gluteal muscle. Body habitus should be assessed before each injection for each patient to ensure that needle length is adequate for IM administration. Injectable naltrexone must be administered only with one of the administration needles supplied in the carton. A spare administration needle of each size is provided in case of clogging.
- Proper IM injection technique is essential. Serious injection-site reactions, sometimes requiring extensive surgical debridement, have been observed with extended-release injectable naltrexone. It has been reported that these severe reactions may be more common if the product is inadvertently administered subcutaneously rather than intramuscularly.
- The medication should be administered every 4 weeks. If a dose is delayed or missed, the next injection should be administered as soon as possible. However, it is not recommended that the medication be readministered at less than 4-week intervals.
- It is not recommended that the medication be administered at a dose higher than 380 mg.

Clinicians are advised to download prescribing information on extended-release naltrexone at http://dailymed.nlm.nih.gov/dailymed/index.cfm.

Special Considerations in Pain Management. As discussed earlier, both oral and extended-release naltrexone block the effects of opioid analgesics. However, pain management for patients using extended-release injectable naltrexone can be even more complicated than for those taking oral naltrexone, because of the long-acting nature of the injectable formulation. In an emergency, regional analgesia, conscious sedation, use of non-opioid analgesics, or general anesthesia may be needed for pain management.[2,63]

Pain management for patients using extended-release injectable naltrexone can be even more complicated than for those taking oral naltrexone, because of the long-acting nature of the injectable formulation.

If regional anesthesia is not used, then a larger amount of the opioid analgesic may be needed to override the opioid blockade. This may result in respiratory depression that is deeper and more prolonged than usual. For this reason, a rapid-onset, short-acting opioid analgesic that minimizes the duration of respiratory depression is preferred. The amount administered should be

titrated to the needs of the patient, who should be monitored closely by trained medical personnel.[1,2]

Initiating Treatment with Acamprosate

Acamprosate typically is initiated 5 days after the cessation of alcohol use. The drug typically reaches full effectiveness in 5 to 8 days.[2,75,76]

Acamprosate therapy should be continued even if a patient relapses to alcohol use.[1]

Treating People with Co-Occurring Disorders

Co-Occurring Psychiatric Disorders. The use of pharmacotherapy in people with co-occurring psychiatric disorders typically involves the following considerations:[30,31,83,84,85]

- Naltrexone and acamprosate may be used in combination with psychiatric medications. There are no known drug interactions between those classes of medication and either drug.
- If a patient exhibits chronic psychiatric symptoms (e.g., depression, mood lability, psychosis, anxiety), concurrent pharmacologic treatment of the alcohol use disorder and the psychiatric comorbidity should be considered.
- If the patient exhibits symptoms of chronic depression or substance-induced depression that limits recovery potential, antidepressant therapy in the absence of contraindications (e.g., a history of mania or hypomania) should be considered.
- Disulfiram is contraindicated in the presence of psychosis because of the risk that it will exacerbate psychotic symptoms.
- Disulfiram may increase blood levels of tricyclic antidepressants and long-acting hepatically metabolized benzodiazepines, thereby increasing the effects of those medications.

Co-Occurring Medical Conditions and Complications. Individuals with alcohol use disorder are at high risk for co-occurring medical conditions as a result of their heavy drinking and greater risk of concurrent drug use (which is particularly problematic if it involves injection drug use), behavioral and social factors such as unprotected sex and homelessness, or lack of regular medical care.[85,86,87] Alcohol can also interfere with balance and coordination, thus predisposing individuals to falls and other injuries. Patients who present to emergency departments and trauma centers with serious injuries are far more likely than members of the general population to have engaged in recent use of alcohol.[88]

Moreover, alcohol affects virtually every organ system. Women are more susceptible to many of the effects of alcohol at lower doses than men because of reduced first-pass metabolism of alcohol and lower average body weights.[89]

MONITORING PATIENT PROGRESS

As is the case with other chronic relapsing disorders, patients diagnosed with an alcohol use disorder require long-term monitoring and support, as well as periodic adjustment of the treatment regimen.

Monitoring

Monitoring patient progress is an ongoing process, during which the patient is assessed on three dimensions: (1) adherence to the treatment plan; (2) ability to maintain abstinence or reduced drinking, duration of periods of abstinence or reduced drinking, and levels of craving; and (3) overall health status and social functioning.[1,3,7] With this information, the clinician can modify the treatment plan, decide whether to continue pharmacotherapy, and address co-occurring medical, psychiatric, and substance use issues.

Sources of Information. Patient self-reports can be useful indicators of treatment progress. In seeking information on treatment progress, it is important for the clinician to avoid conveying a judgmental attitude toward the patient's behavior. Patients should be asked about the quantity and frequency of their drinking, especially during stressful periods (e.g., holidays, celebrations, major life changes). They should be asked about current craving and how they felt over the preceding week (by assigning a rating between 1 and 10, with 1 indicating no craving and 10 the

most intense craving the patient has ever experienced). In addition, patients may be asked whether any episodes have caused particular problems. Identifying patterns of craving over time helps both the patient and the caregiver understand that the pattern of craving fluctuates throughout the day and even over longer periods, indicating the need to continue, adjust, supplement, or discontinue use of a particular medication. Other information that is useful in patient monitoring includes the following:[1,2,13]

- Instruments such as the eight-question *Alcohol Urge Questionnaire* (https://www.phenxtoolkit.org/index.php?pageLink=browse.protocoldetails&id=520301)
- Laboratory tests such as the AST, GGT, CDT, EtG, and urine drug screens
- The patient's record of keeping (or not keeping) appointments for medication monitoring
- The frequency of prescription refills, as monitored through the state PDMP[90] or direct contact with the dispensing pharmacy
- Periodic reports from family members (with a signed release of information form)
- Periodic status reports from specialty substance abuse treatment programs, psychiatric referrals, and other psychosocial therapy or support
- Any information about other drugs being used

In addition to securing the patient's PDMP record, obtaining information from family members and significant others can provide useful perspectives on the patient's behavior and level of function, as does contact with or records from clinicians who have treated the patient in the past and information from the prescription benefit provider.[91] Ultimately, the goal of treatment is to improve the patient's quality of life. Specific areas of patient progress for which the patient should be monitored are described in Table 2.

Adjusting the Treatment Plan

Alcohol use disorder is a chronic illness that, despite treatment, may change in intensity over time.[2,7,13] If a patient begins to experience problems with adherence, the clinician should assess the patient for underlying medical, psychiatric, or social factors and revisit the treatment plan to determine whether different strategies or treatment modalities (pharmacologic and nonpharmacologic) may be useful. For example, increasing the frequency of monitoring visits or counseling may enhance the patient's ability to manage relapse risks or stressors that are contributing to nonadherence, and switching the patient from oral naltrexone to extended-release injectable naltrexone may enhance adherence to the treatment regimen.

A patient's goals may change over time, and the clinician must adapt to new objectives. Also, as with patients who receive treatment for other chronic diseases, patients receiving treatment for alcohol use disorder may relapse. If this occurs, the provider should consider several options:[2,24]

- Examine social, medical, or behavioral factors that contribute to the patient's alcohol consumption
- Increase monitoring
- Adjust the dose of medication
- Increase or change the intensity of psychosocial services
- Refer the patient for specialty care

Determining the Duration of Treatment.

Although the optimal duration of treatment is not known, some evidence suggests that treatment should continue for at least 6 months to 1 year.[2,24]

Because alcohol use disorder is a chronic medical problem, patients may need to use medications for long periods of time or may require multiple episodes of pharmacotherapy. In addition, some patients may benefit from treatment with medication over short periods to help them through particularly stressful situations that may elicit cravings for alcohol (e.g., a patient may ask for disulfiram or naltrexone to use when visiting family members who drink excessively).[2,7]

TABLE 2: Monitoring Health Status and Social Functioning

Areas for Monitoring	Indicators of Progress
Health	• Stabilization of medical problems the patient was experiencing before beginning treatment (e.g., lowered blood pressure; improved liver function; control of blood glucose; and stabilization of asthma, cardiomyopathy, encephalopathy, gastritis, ascites, edema) • Signs of increased attention to personal health, such as seeing physicians or other health care professionals regularly, increased adherence with prescribed medication regimens not related to alcohol treatment (e.g., asthma or blood pressure medications), and healthful lifestyle changes
Mental Status[§]	• Reduced irritability and anxiety • Improved mood • Improved sleep • Obtaining appropriate treatment for anxiety disorders, suicidal ideation, depression, or schizophrenia rather than self-medicating with alcohol
Family/Social Activities	• Increases in positive time spent with loved ones • Reduced interpersonal conflict • Engagement in leisure and recreational activities that do not involve alcohol
Work/School/ Vocational Status	• Resumption of meaningful activities • Gaining employment if previously unemployed • Engagement in school or other employment preparation • Stabilized housing • Improved work or school performance
Legal Status	• Absence of parole or probation violations (in a patient with legal problems) • Absence of new or other legal problems (e.g., driving under the influence charges)

SOURCE: SAMHSA and NIAAA. (2012, September). *Report of the SAMHSA-NIAAA Consensus Panel on New and Emerging Pharmacotherapies for Alcohol Use Disorders and Related Comorbidities*. Rockville, MD: SAMHSA.

Ideally, a decision to discontinue pharmacotherapy will be based on one of the following reasons:[2,13]

- The patient has maintained stable abstinence over a sustained period and reports substantially diminished craving for alcohol.
- The patient feels ready to discontinue the medication.
- The patient is engaged in ongoing recovery activities involving community supports (e.g., attendance at mutual-help group meetings).

Some patients simply stop taking their medication without consulting the prescriber. Or a patient may ask to discontinue medication use because of side effects or other reasons. Still other patients must discontinue medication use because of a significant negative laboratory finding or a problem with their physical health status.[2,13] In each situation, the provider should help the patient withdraw from the medication at an appropriate pace and, as indicated, encourage the patient to continue with psychosocial therapies and participation in mutual-help groups.

Referring a Patient for Higher Levels of Care. If office-based treatment is not effective or the clinician does not have the resources to meet a particular patient's needs, the patient should be referred for more intensive or specialized services.[2,7] Many specialty treatment programs provide services that address not only immediate withdrawal and craving, but also management of long-term abstinence through pharmacotherapy; case monitoring; individual, group, and

[§] It is recommended that the health care professional administer the PHQ-9 screening tool to objectively assess and monitor the patient's mental status over time. http://www.drugabuse.gov/sites/default/files/files/PatientHealthQuestionnaire9.pdf

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family/couples counseling and therapy; other psychosocial services including vocational counseling; and referral to mutual-help groups.[2,24]

A provider who is planning to treat a patient with an alcohol use disorder should become familiar with local treatment resources. Developing relationships with treatment staff members facilitates consultation and referral. In addition, understanding something about a program's treatment duration, modality, philosophy, and continuing-care options helps the provider match a particular patient to an appropriate treatment program.[13] It also helps the provider prepare the patient for what to expect, thus enhancing adherence with a referral.[2]

Providers can find programs in their areas or throughout the United States by using the Behavioral Health Treatment Services Locator on the SAMHSA Web site at http://www.findtreatment.samhsa.gov.

SUMMARY

Medication-assisted treatment has shown much promise in reducing alcohol use and promoting abstinence in patients diagnosed with alcohol use disorder. Considerable research evidence and consensus among experts support the use of pharmacologic treatments in primary care settings.

A number of FDA-approved medications have been shown to be important elements of such treatment. Although some patients do not benefit from medication-assisted treatment, most do. For each patient deemed an appropriate candidate for medication-assisted treatment, multiple pharmacologic agents offer a variety of options so that treatment can be tailored to each patient's needs and circumstances.

As new patient care models are encouraged by the Patient Protection and Affordable Care Act (ACA) and the accompanying improvements in the quality and quantity of treatment options that are anticipated as the ACA is implemented, there is considerable potential for expanding the use of medication-assisted treatment as clinicians recognize their safety, efficacy, and cost-effectiveness.

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APPENDIX A: SOURCES OF HELPFUL INFORMATION

SAMHSA PUBLICATIONS AND WEB SITES

Detoxification and Substance Abuse Treatment, Treatment Improvement Protocol 45
http://www.store.samhsa.gov/product/TIP-45-Detoxification-and-Substance-Abuse-Treatment/SMA13-4131

General Principles for the Use of Pharmacological Agents to Treat Individuals with Co-Occurring Mental and Substance Use Disorders
http://www.ncdsv.org/images/SAMHSA_GeneralPrinciplesUsePharmacologicalAgentsTreatIndividualsCo-OccuringMentalSubstanceUseDisorders_2012.pdf

Incorporating Alcohol Pharmacotherapies Into Medical Practice, Treatment Improvement Protocol 49
http://www.store.samhsa.gov/product/TIP-49-Incorporating-Alcohol-Pharmacotherapies-Into-Medical-Practice/SMA13-4380

Naltrexone for Extended-Release Injectable Suspension for Treatment of Alcohol Dependence, *Substance Abuse Treatment Advisory*
http://www.store.samhsa.gov/product/Naltrexone-for-Extended-Release-Injectable-Suspension-for-Treatment-of-Alcohol-Dependence/SMA07-4267

Opioid Overdose Toolkit
http://www.store.samhsa.gov/shin/content/SMA13-4742/Overdose_Toolkit_2014_Jan.pdf

The Role of Biomarkers in the Treatment of Alcohol Use Disorders, *SAMHSA Advisory*
http://www.store.samhsa.gov/product/The-Role-of-Biomarkers-in-the-Treatment-of-Alcohol-Use-Disorders-2012-Revision/SMA12-4686

SAMHSA's National Registry of Evidence-based Programs and Practices
http://nrepp.samhsa.gov

SAMHSA's Screening, Brief Intervention, and Referral to Treatment (SBIRT)
http://www.samhsa.gov/sbirt

SAMHSA's Treatment Locator
http://www.samhsa.gov/treatment

NIAAA PUBLICATIONS AND WEB SITES

Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide
http://www.niaaa.nih.gov/publications/clinical-guides-and-manuals/alcohol-screening-and-brief-intervention-youth/resources

Assessing Alcohol Problems: A Guide for Clinicians and Researchers, Second Edition
http://www.pubs.niaaa.nih.gov/publications/AssessingAlcohol

Clinical Protocols to Reduce High Risk Drinking in College Students: The College Drinking Prevention Curriculum for Health Care Providers
http://www.collegedrinkingprevention.gov/media/FlemingManual.pdf

Exploring Treatment Options for Alcohol Use Disorders, *Alcohol Alert,* No. 81
http://www.pubs.niaaa.nih.gov/publications/AA81/AA81.htm

Helping Patients Who Drink Too Much: A Clinician's Guide, Updated 2005 Edition
http://www.pubs.niaaa.nih.gov/publications/Practitioner/CliniciansGuide2005/clinicians_guide.htm

Prescribing Medications for Alcohol Dependence
http://www.pubs.niaaa.nih.gov/publications/Practitioner/CliniciansGuide2005/PrescribingMeds.pdf

Rethinking Drinking: Alcohol and Your Health (available in English and Spanish)
http://www.pubs.niaaa.nih.gov/publications/RethinkingDrinking/OrderPage.htm

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MENTORING NETWORK

Providers' Clinical Support System for Medication Assisted Treatment
http://www.pcssmat.org

MUTUAL-HELP GROUPS

Al-Anon Family Groups
http://www.al-anon.alateen.org

Alcoholics Anonymous
http://www.aa.org

Self-Management and Recovery Training
http://www.smartrecovery.org

Women for Sobriety, Inc.
http://www.womenforsobriety.org

WEB-BASED COURSES

ASAM e-Live Learning Center
http://www.softconference.com/asam/default.asp

ASAM From Assessment to Service Planning and Level of Care Course
https://www.changecompanies.net/products/product.php?id=ASE2

ASAM Multidimensional Assessment eLearning
http://www.changecompanies.net/asamcriteria/elearning.php

ASAM SBIRT Core Training Program
http://www.sbirttraining.com

NIAAA Clinician's Guide Online Training
http://www.niaaa.nih.gov/publications/clinical-guides-and-manuals/niaaa-clinicians-guide-online-training

NIAAA Presentations and Videocasts
http://www.niaaa.nih.gov/publications/presentations-and-videocasts

OTHER WEB SITES

American Society of Addiction Medicine
http://www.asam.org

Georgetown University Medical Center's Ensuring Solutions to Alcohol Problems
http://www.ensuringsolutions.org

Gold MS, Aronson, MD. Psychosocial treatment of alcohol use disorder. *Up-to-date* online medical education service, 2013.
http://www.uptodate.com/contents/psychosocial-treatment-of-alcohol-use-disorder

National Association of State Controlled Substances Authorities
http://www.nascsa.org

U.S. Department of Justice, Drug Enforcement Administration, Office of Diversion Control, State Prescription Drug Monitoring Programs
http://www.deadiversion.usdoj.gov/faq/rx_monitor.htm

SUGGESTED INSTRUMENTS FOR SCREENING AND MONITORING

Alcohol Misuse: Screening and Behavioral Counseling Interventions in Primary Care
http://www.uspreventiveservicestaskforce.org/uspstf/uspsdrin.htm

Alcohol, Smoking and Substance Involvement Screening Test (ASSIST)
http://www.who.int/substance_abuse/activities/assist/en/index.html

Alcohol Urge Questionnaire (AUQ)
https://www.phenxtoolkit.org/index.php?pageLink=browse.protocoldetails&id=520301

Alcohol Use Disorders Identification Test (AUDIT)
http://www.whqlibdoc.who.int/hq/2001/WHO_MSD_MSB_01.6a.pdf

Clinical Institute Withdrawal Assessment for Alcohol Scale, Revised (CIWA-Ar)
https://umem.org/files/uploads/1104212257_CIWA-Ar.pdf

Oregon SBIRT Comprehensive Screening and Brief Intervention Resources
http://www.sbirtoregon.org

Problem Oriented Screening Instrument for Teenagers (POSIT)
http://www.emcdda.europa.eu/html.cfm/index4439EN.html

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PUBLISHED GUIDELINES AND REFERENCE TEXTS

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Veterans Health Administration and Department of Defense (DoD). *VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders in the Primary Care Setting.* http://www.healthquality.va.gov/sud/sud_fulltext.pdf

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