Medication for the Treatment of Alcohol Use Disorder: A Brief Guide

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Substance Abuse and Mental Health Services Administration
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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.

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.

‡ 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.