

Treating alcohol dependence: When and how to use 4 medications

Some help patients achieve abstinence, whereas others assist in maintaining sobriety

Mr. G, age 38, is an investment banker referred for evaluation of an alcohol use disorder. Three years ago his internist diagnosed Mr. G with major depression and prescribed a selective serotonin reuptake inhibitor. Mr. G's mood has improved, but his drinking is out of control and is affecting his work and marriage.

Mr. G describes his father as an alcoholic and says he has noticed worrisome similarities in himself. Since his teenage years, he recalls always being able to drink more than his peers. Amnesia episodes began in college during heavy drinking days and now occur almost weekly. Most recently his driver's license was suspended after he was arrested for driving while impaired by alcohol.

He has attempted to stop drinking 3 times in the last 6 months and feels frustrated because he continues to relapse. During his last quit attempt, he remained abstinent for 3 months and believes his mood was unchanged during that time.

For motivated patients such as Mr. G, National Institute on Alcohol Abuse and Alcoholism (NIAAA) guidelines (updated in 2007) consider medications first-line treatment for alcohol dependence, along with psychotherapies and mutual-help groups such as Alcoholics Anonymous.¹ Medications with evidence of efficacy include FDA-approved disulfiram, naltrexone, and acamprosate, and off-label topiramate.

Each drug's pharmacology is different; some may be beneficial during early abstinence, whereas others are more effective for maintaining abstinence. Because many physicians have had little or no experience using



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Alcohol dependence

Clinical Point

During abstinence, substance-induced mood symptoms become less intense whereas primary mood symptoms may not be affected

Box

Alcohol dependence: Diagnostic criteria

Alcohol use disorders describe a maladaptive pattern of alcohol use that causes clinically significant impairment or distress. Alcohol dependence is manifested by ≥ 3 of the following symptoms in a 12-month period:

- **Tolerance**
- **Withdrawal**
- **Often drinking alcohol** in larger amounts or over a longer time period than intended
- **Persistent desire** or unsuccessful efforts to cut down or control alcohol use
- **Spending a great deal of time** in activities necessary to obtain, use, or recover from alcohol's effects
- **Giving up or reducing** important social, occupational, or recreational activities because of alcohol use
- **Continuing alcohol use** despite knowing you have a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol.

Source: Adapted from DSM-IV-TR

these medications,^{2,3} we discuss dosing recommendations and side effect profiles—important clinical differences to guide drug selection and administration.

CASE CONTINUED

Which came first?

When Mr. G presented with depressive symptoms, his internist informed him that alcohol's effects can mimic depression and advised him to cut back his consumption. Mr. G temporarily reduced his drinking but continued to experience depressed mood, sleep disturbances, difficulty concentrating, fatigue, and poor appetite. The internist then prescribed escitalopram, 10 mg/d, and Mr. G says his depressive symptoms improved. He has not attempted suicide or required psychiatric hospitalization.

After a thorough evaluation—including a detailed assessment of his drinking history, other substance use, and mood symptoms—you diagnose Mr. G with alcohol dependence without physiological dependence and a primary major depressive disorder (MDD).

Mr. G's diagnosis of alcohol dependence is based on evidence in the last 12 months of tolerance, repeated loss of control over the amount he drinks, multiple failed attempts to stop drinking, repeated negative consequences to his work productivity and personal relationships, and continued drinking despite knowing that alcohol consumption sometimes intensifies his mood symptoms (*Box*). Physiological dependence is unlikely because he did not experience withdrawal during a recent period of abstinence.

The mood component. Particularly in psychiatric patients, alcohol dependence often coexists with and affects the treatment of other psychopathologies:

- 1 in 3 adults experience an alcohol use disorder during their lifetimes.⁴
- 1 in 3 adults with an alcohol use disorder have a comorbid psychiatric disorder.⁵
- Alcohol dependence doubles the risk of major depression and triples the lifetime risk of any mood disorder.⁴

A thorough evaluation—both medical and psychiatric—is necessary to distinguish a primary mood disorder from a substance-induced mood disorder. Aspects of a patient's history that may support a substance-induced disorder diagnosis include:

- Mood symptoms appear after the onset of a substance use disorder.
- Mood symptoms are absent during abstinence.
- Mood symptoms are consistent with the effects of the drug being used.⁶

Substance-induced mood symptoms usually become less intense and eventually resolve as abstinence is maintained. Primary mood symptoms may not be affected by abstinence, and interventions—including pharmacotherapy—are more likely to be required.

In evaluating Mr. G's drinking history, you determined that his mood symptoms began before he started consuming alcohol regularly and have persisted during periods of abstinence. Thus, primary MDD is a more likely diagnosis than substance-induced MDD.

CASE CONTINUED

Planning treatment

A combination of behavioral therapy and pharmacotherapy is appropriate for treating Mr. G’s alcohol dependence. When you discuss the diagnosis with him, he endorses a goal of abstinence. For behavioral therapy, he says he would like to try Alcoholics Anonymous, which helped a friend “turn his life around.”

He has become accustomed to taking escitalopram once daily but is hesitant to take any medication that requires more frequent dosing. He also worries that medication might impair his work performance, which requires extensive periods of concentration. Your goal—as you consider available medications—is to develop a treatment plan that incorporates Mr. G’s preferences and addresses his concerns.

Disulfiram

Disulfiram, an irreversible aldehyde dehydrogenase inhibitor, is indicated for maintaining enforced sobriety in patients with chronic alcohol dependence (Table 1). Aldehyde dehydrogenase inhibition disrupts alcohol-to-acetate metabolism, which leads to acetaldehyde accumulation. If a disulfiram-treated patient ingests alcohol, increased acetaldehyde levels lead to the unpleasant “disulfiram-ethanol reaction,” with diaphoresis, flushing, nausea, vomiting, headache, tachycardia, and hypotension. The reaction’s severity is proportional to the disulfiram dose and amount of alcohol consumed.

Patients taking disulfiram must abstain from all alcohol, including over-the-counter cold remedies and mouthwashes containing alcohol. Advise patients that ingesting small amounts of alcohol can induce symptoms, even days after taking disulfiram.

Efficacy. Clinical trial results with disulfiram have been mixed. In the largest controlled study to date, Fuller et al⁷ found no significant difference in rates of total abstinence, time to first drink, employment, or social stability measures at 1 year among 605 men who received counseling plus disulfiram, 250 mg/d, or placebo. Other

Table 1

Disulfiram: Fast facts

Table with 1 column and 6 rows: Mechanism, FDA-approved for alcohol dependence, Dosing, Effect, Potential side effects, Contraindications, Comments.

disulfiram studies have found a modest decrease in the frequency of drinking but no effect on abstinence rates.^{8,9}

Because medication adherence is the strongest predictor of outcome with disulfiram,¹⁰ monitoring for adherence and stressing its importance to patients may increase the drug’s efficacy. Disulfiram may be most effective in highly motivated patients with stable social support or as an adjuvant to an outpatient treatment program.

Administration. Disulfiram is available in 250-mg tablets and is usually dosed from 125 to 500 mg/d. Treatment can begin after patients abstain from alcohol for ≥12 hours and have a serum alcohol concentration of zero.

Side effects. Drowsiness is a common complaint with disulfiram; this adverse effect is frequently self-limited and can be reduced by evening dosing.

Subclinical liver enzyme elevations have been reported in 25% of patients taking disulfiram.¹¹ Although rare, potentially fatal hepatotoxicity has been reported^{12,13} (with a dose as low as 200 mg/d¹²), typically occurring early in treatment and associated with jaundice and fever. One study estimated the risk of dying of hepatotoxicity caused by disulfiram to be 1 in 30,000 patients/year.¹⁴

Clinical Point

Drowsiness, a common complaint with disulfiram, is often self-limited and can be reduced by evening dosing



Alcohol dependence

Clinical Point

Naltrexone's effect might have a genetic component, as suggested by greater benefit in persons with a family history of alcoholism

Table 2

Naltrexone: Fast facts

Mechanism: Opioid receptor antagonism interferes with β -endorphin pathways
FDA-approved for alcohol dependence: Yes
Dosing: Oral 50 mg once daily (recent evidence suggests safety and efficacy at 100 mg once daily); IM 380 mg once every 4 weeks
Effect: Decreases frequency and severity of relapse
Potential side effects: Nausea, myalgia, headache, dizziness
Contraindications: Opioid use, acute hepatitis, liver failure
Comments: Monitor liver function; once-monthly dosing may improve adherence

A recent Swedish study¹³ reviewed data from 1966 through 2002 and found 82 cases of drug-induced liver injury associated with disulfiram. By comparing these findings with sales figures from 1972 to 2002, the authors report an incidence of disulfiram-induced liver injury of about 1 case per 1.3 million estimated average daily doses.

Order liver function tests at baseline, then retest 10 to 14 days after starting disulfiram and again approximately 4 weeks later. Thereafter, monitoring once every 3 to 6 months is generally sufficient in patients without liver disease symptoms.

Other serious adverse events associated with disulfiram therapy include optic neuritis, peripheral neuritis, cholestatic hepatitis, seizures, and arrhythmias. Psychosis also can occur, generally with dosages ≥ 500 mg/d. Avoid concomitant use of disulfiram and metronidazole, which can cause acute psychosis.

Disulfiram-related inhibition of cytochrome P-450 can increase serum levels and toxicity risk of medications metabolized in the liver, such as warfarin, phenytoin, and isoniazid. Patients taking concomitant warfarin and disulfiram require close monitoring for increases in the international normalized ratio (INR).

Contraindications. Disulfiram is contraindicated in patients with ischemic heart

disease and those who are pregnant. Also avoid disulfiram in patients with cerebrovascular disease, diabetes mellitus, psychosis, or cognitive impairment.

Recommendation. Disulfiram is a valid option for treating alcohol dependence in a select group of highly motivated patients who are medically and psychiatrically stable and in whom adherence can be closely monitored.

Naltrexone

Naltrexone is a μ -opioid receptor antagonist thought to reduce alcohol's reinforcing effects by interfering with β -endorphin pathways. It is indicated for treating alcohol dependence and has been shown to reduce relapse and number of drinking days in alcohol-dependent patients (Table 2).¹⁵

Naltrexone also has reduced alcohol consumption in healthy volunteers, social drinkers, and other nondependent drinkers.¹⁶ Its effect may have a genetic component, as suggested by greater benefit in persons with a family history of alcoholism.¹⁷

Efficacy. Most studies investigated naltrexone as part of a comprehensive treatment program that included behavioral therapies.¹⁸ Recently, the randomized, placebo-controlled Combining Medications and Behavioral Interventions (COMBINE) study found that using either naltrexone or behavioral therapy improved abstinence, and combining naltrexone with behavioral therapy was not more effective than either treatment alone.¹⁹

Administration. Oral naltrexone is usually started at 25 mg and increased over 2 to 3 days to 50 or 100 mg/d. The standard dose is 50 mg/d, although the COMBINE study reported efficacy at 100 mg/d.¹⁹

Oral naltrexone is most helpful for patients who adhere to 70% to 90% of the medication.²⁰ The extended-release form (a 380-mg IM dose given every 4 weeks) provides an option to monitor adherence.²¹

Side effects. Naltrexone toxicity can cause hepatocellular injury. Do not administer

this drug to patients with acute hepatitis or end-stage liver disease. When prescribing naltrexone, check patients' liver function monthly for the first 3 months, then once every 3 months thereafter.²² Less serious, common side effects include nausea, myalgia, and headache.

Naltrexone antagonizes opioid receptors and causes withdrawal symptoms in patients who are physically dependent on opioids. Therefore, do not give naltrexone to patients who require opioids for chronic pain. If your patient is using an opioid but could switch to other pain medication, discontinue the opioid for at least 7 days and consider a urine toxicology or naltrexone challenge before starting naltrexone.

Urine drug tests are inexpensive and easy to use but have limitations. Many standard "dipsticks" will detect heroin, morphine, and codeine but not oxycodone, hydrocodone, or other synthetic opioids. Specific tests are available to detect oxycodone, hydrocodone, hydromorphone, buprenorphine, and methadone. Some synthetic opioids (such as fentanyl) remain difficult to detect, however, because of their low concentration and rapid metabolism.

Acamprosate

Acamprosate is structurally similar to gamma-aminobutyric acid (GABA) and is thought to inhibit the glutamatergic system. This attenuation by acamprosate reduces the glutamatergic hyperactivity normally seen after chronic alcohol exposure.

Acamprosate is indicated for relapse prevention in patients with alcohol dependence who have stopped drinking (*Table 3*). Multiple randomized studies have demonstrated its efficacy in improving abstinence rates as compared with placebo.^{23,24} Other studies, however, failed to show improved abstinence with acamprosate.²⁵ Some of the negative studies included patients who recently relapsed or had only a few days of abstinence before starting acamprosate.^{19,26} Therefore, acamprosate might be most effective when used to maintain abstinence and less effective—if at all—to initiate abstinence.

Table 3

Acamprosate: Fast facts

Mechanism: Structurally similar to GABA; thought to inhibit the glutamatergic system
FDA-approved for alcohol dependence: Yes
Dosing: 666 mg tid
Effect: Increases abstinence
Potential side effects: Nausea, diarrhea, suicidal thoughts
Contraindications: Severe renal disease
Comments: Monitor patients for suicidal thoughts and depression

Administration. Acamprosate is available in 333-mg tablets, with a recommended dosage of 666 mg tid. Side effects tend to be transient and mild. Reduce the dose to 333 mg tid for patients with moderate renal insufficiency (creatinine clearance [CrCl] 30 to 50 mL/min), and do not use acamprosate in patients with severe renal insufficiency (CrCl < 30 mL/min).

Side effects. Acamprosate was well-tolerated in clinical trials; diarrhea and other GI side effects were the most commonly reported adverse events.

In some placebo-controlled studies, patients taking acamprosate reported more frequent suicidal thoughts and attempts compared with patients taking placebo.²⁷ These events were extremely rare, and no direct relationship with acamprosate therapy has been established. Nonetheless, monitor patients for depression and suicidal thoughts during acamprosate therapy.

Topiramate

Topiramate potentiates GABA and inhibits excitatory glutamate transmission—properties believed to lead to decreased dopamine release at the nucleus accumbens in response to alcohol consumption. Although topiramate is not FDA-approved for alcohol dependence, limited data comparing this anticonvulsant with placebo have shown a reduction in drinking and increased abstinence (*Table 4, page 36*).^{28,29}

Clinical Point

Acamprosate might be most effective when used to maintain abstinence and less effective—if at all—to initiate abstinence



Alcohol dependence

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Limited data comparing topiramate with placebo found a reduction in drinking and increased abstinence

Table 4

Topiramate: Fast facts

Mechanism: Potentiates GABA and inhibits glutamate receptor subtypes
FDA-approved for alcohol dependence: No
Dosing: 300 mg/d in divided doses
Effect: Decreases craving and drinking
Potential side effects: Metabolic acidosis, psychomotor slowing, dizziness, difficulty concentrating, paresthesia, weight loss, nephrolithiasis, hyperammonemia with concomitant use of valproic acid
Contraindications: None known other than hypersensitivity (as with all drugs)
Comments: Dose titration requires several weeks; avoid abrupt withdrawal; may reduce effectiveness of oral contraceptives

Administration. Start with 25 mg/d and increase over several weeks to 300 mg/d, given in divided doses.

Side effects include dizziness, paresthesia, somnolence, difficulty concentrating, and weight loss. Because topiramate is excreted renally, reduce doses by 50% in patients with CrCl <70 mL/min. Hyperammonemia with or without encephalopathy has been associated with concomitant use of valproic acid, even in patients who have tolerated either drug alone.

Other renal side effects include an elevated risk of nephrolithiasis. Topiramate's inhibition of carbonic anhydrase can reduce bicarbonate levels, leading to a non-anion gap metabolic acidosis.

CASE CONTINUED

Implementing a treatment plan

You start Mr. G on oral naltrexone, 25 mg/d, and titrate to 100 mg/d. Although no optimum treatment duration has been established, you plan to follow NIAAA recommendations that Mr. G use naltrexone at least 3 months, with the possibility of continuing 1 year or longer if he responds well.¹

You schedule weekly visits for the first month to monitor for side effects and to make any necessary modifications in behavioral and pharmacologic treatment. You also

continue escitalopram, 10 mg, which has successfully controlled Mr. G's MDD symptoms.

Medications for alcohol dependence generally have been studied as adjuncts to behavioral therapies. The COMBINE study of 1,383 alcohol-abstinent patients found naltrexone with medical management or cognitive-behavioral therapy alone to be equivalent in efficacy.¹⁹ The medical management provided a supportive environment, encouraged medication compliance, provided empathy to build a therapeutic relationship, and promoted self-help groups as an adjunct to treatment.³⁰ Thus, medication has a role in treating alcohol dependence, but behavioral therapy remains an important part of comprehensive substance abuse treatment.

When choosing medications, consider the agents' clinically relevant differences:

- Naltrexone and—less conclusively—topiramate have shown benefit for alcohol-dependent patients starting treatment and for relapse prevention.
- Acamprosate may help prevent relapse in abstinent patients.
- Disulfiram remains a valid option in highly motivated patients with social support available to ensure medication adherence.

Because Mr. G is starting therapy after recent alcohol use, medications such as naltrexone and topiramate that have shown benefit early in treatment (in addition to relapse prevention) are preferred. Of these 2 drugs, naltrexone is the better choice for Mr. G—who is concerned about his work performance—because difficulty concentrating is a common side effect of topiramate. Oral naltrexone would be preferred as initial therapy for Mr. G because he has expressed comfort taking once-daily oral medication. The more expensive once-monthly naltrexone depot formulation could be a second-line treatment if adherence becomes an issue.

Hypersensitivity is considered a contraindication for any medication. Mr. G tolerates well an initial dose of 25 mg/d, followed by increases to 50 mg and then 100 mg over several days. You titrate oral naltrexone to 100 mg/d—even though it

is commonly prescribed at 50 mg/d—because recent evidence suggests efficacy and safety at the higher dosage.¹⁹

References

1. National Institutes of Health. *Helping patients who drink too much: a clinician's guide*. Bethesda, MD: National Institute on Alcohol Abuse and Alcoholism; 2007. NIH Publication 07-3769. Available at: <http://www.niaaa.nih.gov/Publications/EducationTrainingMaterials/guide.htm>. Accessed January 3, 2008.
2. Substance Abuse and Mental Health Services Administration. *National Survey of Substance Abuse Treatment Services: 2005. Data on substance abuse treatment facilities, (DASIS Series: S-34)*. Rockville, MD: Office of Applied Studies, 2006. DHHS Publication (SMA) 06-4206.
3. Substance Abuse and Mental Health Services Administration. *Treatment episode data set (TEDS) highlights 2005: National admissions to substance abuse treatment services*. Rockville, MD: Office of Applied Studies, 2006. DHHS Publication (SMA) 07-4229.
4. Hasin DS, Stinson FS, Ogburn EO, Grant BF. Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States. *Arch Gen Psychiatry* 2007;64(7):830-42.
5. Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) study. *JAMA* 1990;264(19):2511-8.
6. Mariani JJ, Levin FR. Treatment of comorbid conditions of substance abuse. *Directions in Psychiatry* 2005;25(2):129-39.
7. Fuller RK, Branchey L, Brightwell DR, et al. Disulfiram treatment of alcoholism. A Veteran's Administration cooperative study. *JAMA* 1986;256:1449-55.
8. Fuller RK, Roth HP. Disulfiram for the treatment of alcoholism. An evaluation of 128 men. *Ann Intern Med* 1979;90:901-4.
9. Schuckit MA. A one-year follow-up of men alcoholics given disulfiram. *J Stud Alcohol* 1985;46:191-5.
10. Collins GB, McAllister MS, Adury K. Drug adjuncts for treating alcohol dependence. *Cleve Clin J Med* 2006;73(7):641-4.
11. Goyer PF, Major LF. Hepatotoxicity in disulfiram treated patients. *J Stud Alcohol* 1979;40:133-7.
12. Ranek L, Buch Andreasen P. Disulfiram hepatotoxicity. *Br Med J* 1977;2(6079):94-6.
13. Björnsson E, Nordlinder H, Olsson R. Clinical characteristics and prognostic markers in disulfiram-induced liver injury. *J Hepatol* 2006;44(4):791-7.
14. Enghusen PH, Loft S, Anderson JR, et al. Disulfiram therapy—adverse drug reactions and interactions. *Acta Psychiatr Scand* 1992;86(369):59-66.
15. Volpicelli JR, Volpicelli LA, O'Brien CP. Medical management of alcohol dependence: clinical use and limitations of naltrexone treatment. *Alcohol Alcohol* 1995;30:789.
16. de Wit H, Svenson J, York A. Non-specific effect of naltrexone on ethanol consumption in social drinkers. *Psychopharmacology (Berl)* 1999;146:33.
17. Monterosso JR, Flannery BA, Pettinati HM, et al. Predicting treatment response to naltrexone: the influence of craving and family history. *Am J Addict* 2001;10:258-68.
18. Srisurapanont M, Jarusuraisin N. Opioid antagonists for alcohol dependence. *Cochrane Database Syst Rev* 2005;(1): CD001867.
19. Anton RF, O'Malley SS, Ciraulo DA, et al. Combined pharmacotherapies and behavioral interventions for alcohol

Related Resources

• National Institutes of Health. *Helping patients who drink too much: a clinician's guide*. Bethesda, MD: National Institute on Alcohol Abuse and Alcoholism; 2007. NIH Publication 07-3769. www.niaaa.nih.gov/Publications/EducationTrainingMaterials/guide.htm.

• American Society of Addiction Medicine. www.asam.org.

• American Academy of Addiction Psychiatry. www.aaap.org.

Drug Brand Names

Acamprosate • Campral	Naltrexone,
Disulfiram • Antabuse	extended-release • Vivitrol
Escitalopram • Lexapro	Topiramate • Topamax
Naltrexone, oral • ReVia	Valproic acid • Depakote

Disclosure

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dependence: the COMBINE study: a randomized controlled trial. *JAMA* 2006;295:2003-17.

20. Monti PM, Rohsenow DJ, Swift RM, et al. Naltrexone and cue exposure with coping and communication skills training for alcoholics: treatment process and 1-year outcomes. *Alcohol Clin Exp Res* 2001;25:1634-47.
21. Garbutt JC, Kranzler HR, O'Malley SS, et al. Efficacy and tolerability of long-acting injectable naltrexone for alcohol dependence: a randomized controlled trial. *JAMA* 2005;293(13):1617-25.
22. Doering PL. Substance-related disorders: alcohol, nicotine, and caffeine. In: DiPiro JT, Talbert RL, Yee GC, et al, eds. *Pharmacotherapy: a pathophysiologic approach*. 4th ed. Stamford, CT: Appleton & Lange; 1999.
23. Mann K, Lehart P, Morgan MY. The efficacy of acamprosate in the maintenance of abstinence in alcohol-dependent individuals: results of a meta-analysis. *Alcohol Clin Exp Res* 2004;28(1):51-63.
24. Paille FM, Guelfi JD, Perkins AC, et al. Double-blind randomized multicentre trial of acamprosate in maintaining abstinence from alcohol. *Alcohol Alcohol* 1995;30:239-47.
25. Chick J, Howlett H, Morgan MY, Ritson B. United Kingdom Multicentre Acamprosate Study (UKMAS): a 6-month prospective study of acamprosate versus placebo in preventing relapse after withdrawal from alcohol. *Alcohol Alcohol* 2000;35(2):176-87.
26. Mason BJ, Goodman AM, Chabac S, Lehart P. Effect of oral acamprosate on abstinence in patients with alcohol dependence in a double-blind, placebo-controlled trial: the role of patient motivation. *J Psychiatr Res* 2006;40(5):383-93.
27. Mason BJ. Treatment of alcohol-dependent outpatients with acamprosate: a clinical review. *J Clin Psychiatry* 2001;62(suppl 20):42-8.
28. Johnson BA, Ait-Daoud N, Bowden CL, et al. Oral topiramate for treatment of alcohol dependence: a randomised controlled trial. *Lancet* 2003;361(9370):1677-85.
29. Johnson BA, Rosenthal N, Capece JA, et al. Topiramate for treating alcohol dependence: a randomized controlled trial. *JAMA* 2007;298(14):1641-51.
30. COMBINE Study Research Group. Testing combined pharmacotherapies and behavioral interventions in alcohol dependence: rationale and methods. *Alcohol Clin Exp Res* 2003;27:1107-22.

Clinical Point

Medication has a role in treating alcohol dependence, but behavioral therapy remains important in substance abuse treatment as well

Bottom Line

Medications such as disulfiram, naltrexone, acamprosate, and topiramate can be useful adjuncts to behavioral therapy when treating alcohol dependence. Some help more to initiate abstinence and others to maintain abstinence. To promote adherence to these medications, consider the patient's history, comorbidities, and preferences when developing a comprehensive substance abuse treatment plan.