Alcohol Use Disorders and Psychiatric Comorbidity: 
Pharmacological Management

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There is increasing evidence and support for medications for alcohol use disorders to be used in regular clinical practice, and not to be limited to specialty substance abuse settings. Here, special considerations for pharmacological management.

Alcohol misuse and alcohol use disorders (AUDs) continue to be an ongoing problem in the US. An estimated 52% of the population reports current alcohol use, and while many people use alcohol responsibly, a significant number transition to heavy drinking, which is associated with an increase in health risk and risk of AUDs.¹ On the basis of a large epidemiological study (National Epidemiologic Survey of Alcohol and Related Conditions, or NESARC), it is estimated that 17.6 million Americans suffer from an AUD.² Individuals with an AUD are more likely than the general population to have coexisting psychiatric disorders. NESARC data show that psychiatric disorders independent of acute intoxication and withdrawal but associated with an AUD are among the most prevalent in the US. This has important clinical implications and suggests that screening and treatment of comorbid conditions should be a national priority.

Mood and anxiety disorders are the most common comorbidities in patients with AUDs.³ There are high rates of comorbid AUDs among psychiatric patients: highest prevalence is among those with bipolar disorder.⁴ Rates of AUDs are also higher among patients with serious mental illness and among military veterans with PTSD than among the general population.⁴,⁵ Clearly, adequate screening for psychiatric disorders among those who present for treatment or screening for an AUD is of high importance in all clinical settings.

Pharmacological management
Pharmacotherapy is the first line of treatment for most psychiatric disorders and substance use disorders (SUDs). Pharmacotherapy to treat AUDs, while far from standard, should be available to patients who want it. Pharmacological management is often available in settings where psychotherapy is not; medications can be incorporated easily into a comprehensive treatment plan that includes psychosocial interventions.

There are special clinical considerations that are important when treating comorbidity. Use of medications to treat an AUD is not widespread, and some clinicians—particularly those without an addiction background—may be reluctant to prescribe medications for psychiatric patients. Clinicians may be concerned about drug-alcohol interactions. Fortunately, there is a growing body of literature as well as medication guidelines that may help guide clinicians incorporate medications for AUDs into their practice.

Drug therapy for AUDs
There are 4 medications approved by the FDA to treat AUDs: disulfiram, naltrexone, acamprosate, and naltrexone long-acting formulation. The anticonvulsant topiramate should also be mentioned as the medication with the most promise in treating AUDs, although it has not been formally approved by the FDA for this indication.

While research into medications designed to treat AUDs have historically excluded psychiatric comorbidities, in “real-world” clinical settings, comorbidity is often the norm rather than the exception. Most studies in individuals with psychiatric comorbidity have been conducted with naltrexone. Naltrexone is an opioid antagonist that was approved by the FDA in 1994 to treat AUDs. Naltrexone is thought to decrease the reinforcing aspects of alcohol and perhaps to decrease craving. Its efficacy in reducing excessive drinking has been confirmed in several meta-analyses.⁶ Well-designed studies have confirmed the safety and efficacy of naltrexone in patients who have depression,⁷-⁹ PTSD,¹⁰,¹¹ and even serious mental illness.¹²,¹³ Intramuscular naltrexone may be particularly useful in patients with serious mental illness, in whom medication adherence may be an issue; there is at least some evidence of its usefulness in this...
population (personal correspondence). In these aforementioned studies, patients were able to safely take naltrexone concurrently with psychiatric medications. There is also some evidence that in depressed patients with an AUD, adequate treatment of both the psychiatric disorder and the AUD with naltrexone is more effective than treating each disorder alone.8

Disulfiram has been around the longest. It acts as an inhibitor of acetaldehyde dehydrogenase; if alcohol is consumed, it blocks the metabolism of alcohol, causing a buildup of acetaldehyde, which causes a severe and unpleasant reaction. Many clinicians and patients are reluctant to use this medication because of the potential for a disulfiram-alcohol reaction, and its use is hampered by poor adherence. Nevertheless, for some patients, disulfiram can be a powerful deterrent to drinking. Several reports and studies have shown that disulfiram can be used safely in patients with a number of comorbid disorders, including serious mental illness.7

Disulfiram can be incorporated into a comprehensive treatment plan of medication and psychotherapy for the comorbid condition, such as PTSD.14 Early reports described the potential for disulfiram-induced psychosis, but this occurred at much higher dosages (1000 to 2000 mg/d) than those used today (250 mg/d). Nevertheless, for this reason, and because of the potential for a disulfiram-alcohol reaction, disulfiram should be used carefully in psychiatric patients and care should be given to those with potential for psychosis, impulsivity, and cognitive deficits. Acamprosate, approved by the FDA in 2004, is useful for promoting abstinence. It is well tolerated; GI adverse effects are the most common. It is also unique among the FDA-approved medications in that it is not metabolized in the liver, so it can be given safely to patients with liver disease; however, it should be used with caution in those with kidney disease. Acamprosate has been used safely even in those with serious mental illness for whom psychiatric medications were also prescribed.15

Finally, the anticonvulsant topiramate has promise in treating alcohol dependence.16 Topiramate can be initiated while the patient is still drinking, and its potential to treat psychiatric symptoms such as depression and anxiety make it attractive for patients with comorbid conditions. It is currently being tested in individuals with an AUD and comorbid PTSD or comorbid bipolar disorder (see: www.ClinicalTrials.gov). However, its adverse-effect profile, which may include cognitive deficits, suggests that it might not be the best choice for patients with serious psychiatric disorders, such as schizophrenia.

**Conclusion**

Despite growing evidence, medications for AUDs continue to be under-prescribed—even in settings that include treatment for both psychiatric disorders and SUDs and easy access to pharmacotherapy (such as VA settings).17,18 However, there is increasing evidence and support for these medications to be used in regular clinical practice and not to be limited to specialty substance abuse settings. For those interested in using these medications, publications such as those provided by the Substance Abuse and Mental Health Services Administration are useful guides.19

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**Disclosures:**

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**References:**


