Medications for Substance Use Disorder Treatment

Alcohol Use Disorder Treatment Medications

FDA-Approved

Naltrexone is effective in reducing heavy drinking when used in the oral form (50mg/day) or the long-acting injectable form (Vivitrol®, 380 mg monthly). It reduces craving for alcohol and makes drinking alcohol less pleasurable. It is a mu-opioid antagonist which precludes its use in patients who take opioids. It can occasionally cause hepatic impairment and should be used cautiously in patients with liver disease.

Acamprosate (Campral®) is administered as an oral medication (666 mg TID), and acts at the GABA and glutamate receptors. It appears to be most effective for maintaining abstinence, rather than decreasing heavy drinking. It decreases post-withdrawal anxiety. It can be used in patients with significant liver disease but is renally excreted and contraindicated in renal failure.

Disulfiram (Antabuse®) acts by causing unpleasant symptoms when alcohol is consumed. The medication interrupts the normal metabolism of alcohol and causes a build-up of acetaldehyde, which produces symptoms of nausea, vomiting, flushing, dyspnea, among others. A typical dose is 250 mg daily. Care must be taken to avoid all forms of alcohol (e.g. in mouthwash) in order to avoid symptoms. It is contraindicated in patients with severe coronary disease or psychosis. It works best when supervised daily administration of the medication is provided, in order to avoid non-adherence.

Off-label

Topiramate acts at both GABA and glutamate receptors and is associated with both a decrease in heavy drinking days and an increase in the number of days abstinent. The dose is slowly titrated up from 25 mg per day to a maximum of 150 mg po BID. It may be started while patients are still drinking and can cause a gradual reduction in intake. Side effects include mental slowing, weight loss and paresthesias.

Gabapentin is thought to act as a calcium modulator at presynaptic terminals inhibiting the release of glutamate. Its use is associated with increased rates of abstinence and a decrease in heavy drinking. The preferred dose is 1800 mg/day. Side effects include sedation and dizziness. Some evidence suggests that combining naltrexone and gabapentin is helpful in improving naltrexone adherence and decreasing insomnia and may be more effective than either medication alone.

Medications for Substance Use Disorder Treatment

Opioid Use Disorder Treatment Medications

Methadone is a mu-opioid agonist and is an effective medication for OUD. Its use is associated with a reduction in injection drug use, mortality, costs of care, crime, and risk of HIV and hepatitis C transmission. In the US methadone must be dispensed from an Opioid Treatment Program (OTP) approved by the federal government; it is illegal for office-based providers to prescribe methadone for treatment of OUD. Canadian physicians can take additional training and gain the ability to prescribe methadone for OUD from their offices. Other countries have varying regulations regarding methadone. The starting dose is up to 30 mg per day which is gradually increased to the effective dose of typically 60-120 mg per day. The medication is dispensed daily and under direct observation, but eventually patients may qualify for "take-homes." There is a risk of overdose if the dose is raised too quickly or if the medication is diverted and taken in large doses, especially when combined with other opioids or sedative-hypnotics. Side effects include sedation, constipation, and (rarely) prolongation of the QT interval leading to an increased risk of torsades de pointes ventricular tachycardia.

Buprenorphine is also a mu-opioid agonist and an effective medication for OUD. It is available in several formulations and includes combination products (buprenorphine and naloxone) and mono-products (buprenorphine alone). The combination forms are oral transmucosal products and are available as generic and proprietary formulations (Suboxone®, Zubsolv®, and Bunavail®). Mono-products are available as a generic taken sublingually, subdermal implantable rods which last six months (Probuphine®), and a monthly injectable (Sublocade®).

Treatment with buprenorphine is also associated with a reduction in injection drug use, mortality, costs of care, crime, and risk of HIV and hepatitis C transmission. In the US, buprenorphine products can only be prescribed by providers who have obtained a federal waiver from the DEA. Physicians, nurse practitioners and physician assistants may obtain this waiver by completing a requisite number of hours of training (8 for physicians, 24 for NPs and PAs). This training may be completed online through an approved organization such as ASAM (https://elearning.asam.org/) or the American Academy of Addiction Psychiatry (AAAP). Buprenorphine has a very low risk of respiratory depression unless combined with sedative/hypnotic agents.

Naltrexone is an opioid antagonist that is largely ineffective for OUD in the oral form, but there is evidence for its use to decrease relapse in OUD when administered as a long-acting intramuscular injection (Vivitrol®). Each injection is effective for 4 weeks, and acts by blocking the effect of other opioids during that period. Starting patients on naltrexone can be challenging because they must be abstinent from opioids between 2-10 days prior to starting the medication in order to avoid precipitated withdrawal. Once a patient is receiving naltrexone, they appear to have a relapse rate that is similar to that of patients treated with buprenorphine or methadone. however, unlike these two medications, naltrexone does not appear to be associated with decreased mortality and patients typically continue naltrexone for a much shorter time.

Medications for Substance Use Disorder Treatment

Tobacco Use Disorder Treatment Medications

FDA-Approved

Combined Nicotine replacement therapies (NRT) are available in many forms including a long-acting daily patch and several short-acting options. These are most effective when used in combination, with the patch providing baseline control of nicotine withdrawal symptoms and the short-acting agents addressing craving and breakthrough withdrawal symptoms. Patches, gum, and lozenges are available over the counter, while the nasal spray and oral inhaler require prescription. People who smoke > 10 cigarettes (1/2 pack) per day should start with the highest dose patch (21 mg) and taper the dose over 10 weeks. Those who smoke less should start with the 14 mg patch. Patients should also use a short acting form of NRT concurrently. Starting treatment with more than one daily patch (plus a short acting agent such as gum or lozenges) may be appropriate for patients who smoke more than 1 pack per day.

Varenicline (Chantix®) is a partial agonist at the nicotinic acetylcholine receptor. It is initiated at a dose of 0.5 mg/day and rapidly titrated to the effective dose of 1 mg BID. It should be started at least one week before the planned quit date and continued for 12 weeks or longer. Administration with food and water reduces the risk of nausea. There is some mixed evidence that it is associated with neuropsychiatric symptoms, although the FDA has removed the boxed warning with regards to serious neuropsychiatric events. Its use is not recommended in patients who are psychotic or markedly mentally unstable. Recent data also suggest that use of varenicline may intensify the intoxicating effects of alcohol. Follow up monitoring should be arranged for all patients within one week of starting treatment.

Bupropion (Zyban®) is also used as an anti-depressant that works by enhancing noradrenergic and dopaminergic release. Compared with other medications used for smoking cessation, bupropion is associated with less short-term weight gain; however, this appears to be a temporary effect. Treatment is initiated at dose of 150 mg daily for the first three days and then increased to 150 mg BID. Although usually treatment lasts for 4 weeks, treatment may be continued for up to a year. Bupropion decreases the seizure threshold and may also be associated with neuropsychiatric symptoms. Follow up monitoring should be arranged for all patients within one week of starting treatment.

Off-label

Nortriptyline is a tricyclic antidepressant but the exact mechanism of action for smoking cessation is unknown. Nevertheless, it has been effective regardless of comorbid depression. The dosing is similar to that for the treatment of depression and blood levels should be checked when a steady state has been reached. The initial dose is 25 mg/day initiated between 10-28 days before quit date with a gradual increase to 75-100 mg/day over 10 days to 5 weeks. The course of treatment is 12 weeks. The medication should then be gradually tapered to prevent discontinuation side effects. Due to the anticholinergic effects, exercise caution in the elderly and those with cardiovascular disease.

Clonidine is a centrally acting alpha-agonist hypotensive agent that is effective in smoking cessation. The exact mechanism of action is unknown. The dose ranges from 0.15–0.75 mg/day by mouth and from 0.10–0.20 mg/day transdermal (TTS). There is no clear dose response relationship. Initial dosing is typically 0.10 mg BID orally or 0.10 mg/day TTS, increasing by 0.10 mg/day per week if needed. The treatment duration ranges from 3–10 weeks. Smoking cessation should be initiated between 0 to 3 days after starting the medication. Patients should be cautioned not to stop the medication abruptly due to rebound hypertension. The most significant side effects include dry mouth, sedation, dizziness, and constipation.