Medication for Addiction Treatment: A Guide for Primary Care Providers[1]

Medication	Uses	Maintenance dosing	Side effects and risks	Precautions	Notes
Alcohol use disorder*					
Oral naltrexone	Maintenance	50 mg/day by mouth	Nausea, headache, dizziness, elevated transaminases	Contraindicated if any chronic opioid treatment, or with AST or ALT > 5 times the upper limit of normal; use carefully and with specialty input on risk/benefit ratio in decompensated cirrhosis due to impaired metabolism in liver disease. Periodic monitoring of liver function tests (LFTs) is recommended.	
Intramuscular (IM) naltrexone	Maintenance	380 mg IM every four weeks	Nausea, fatigue, dizziness, injection site reaction	Periodic monitoring of LFTs is recommended. Impaired metabolism in liver disease.	May start with oral formulation to ensure tolerability
Acamprosate	Maintenance	666 mg by mouth three times daily	Diarrhea, nervousness, fatigue	Contraindicated with creatinine clearance </= 30 ml/min; reduce dose in creatinine clearance 30-50 ml/min.	Safe in decompensated liver disease.
Disulfiram	Maintenance	Weeks 1-2: 500 mg by mouth daily Thereafter: 250 mg by mouth daily	Drowsiness, metallic taste, headache, peripheral neuropathy, rare fulminant hepatitis	Do not administer until the patient has been abstinent from alcohol for at least 12 hours as causes highly unpleasant adversive reaction. Contraindicated in severe myocardial disease or known coronary occlusion; psychosis; pregnancy; or with allergies to rubber, nickel or cobalt.	Unlikely to be effective outside of highly structured settings or in patients highly motivated for self-change.
Opioid use disorder					
Methadone	Inpatient withdrawal management; maintenance	Most effective at doses of 60 mg or more by mouth daily.	Sedation, prolongation of the QTc interval, nausea, constipation, weight gain, edema, amenorrhea, decreased bone	Prolonged, variable half-life with incomplete cross tolerance with other opioids requires low initiation dose (30mg or less) and slow titration (10mg or less dose increases every 3 days or longer). Potential for drug interactions with inducers or inhibitors of P450 system. Obtain baseline EKG in those with risk factors for QTC prolongation; dose reduction and	Schedule II substance in US. For outpatient addiction treatment, only available through state-licensed programs. For pain treatment, available from licensed prescribers.

			density, decreased libido. Risk of respiratory depression and overdose.	EKG monitoring or alternative treatment is recommended for patients with QTC ≥ 500 msec.	
Transmucosal buprenorphine-naloxone (sublingual or buccal)	Inpatient withdrawal management; induction; maintenance	Usual maintenance dose range: *Sublingual film or tablet*--Buprenorphine 4mg/naloxone 1mg to buprenorphine 24mg/naloxone 6 mg sublingually daily (dose range varies for non-generic formulations); *Buccal film*-- Buprenorphine 2.1mg/naloxone 0.3mg to buprenorphine 12.6-naloxone 2.1mg once daily.	Nausea, constipation, headache, insomnia. Rarely associated with overdose, usually in combination with other sedating agents.	Risk of precipitated opioid withdrawal if initiated too soon in opioid-tolerant patient after last use of full opioid agonist; patients should be experiencing at least moderate withdrawal at first dose (typically 12 or more hours after last heroin, more for longer acting agents) and patients using primarily fentanyl may require low-dose initiation ("micro-dosing")[2]. May be less effective in severe liver disease due to increased bioavailability of naloxone. Periodic monitoring of LFTs is recommended.	Schedule III. As of January 2023, the requirement for a specific DEA waiver to prescribe buprenorphine for more than 30 patients was removed, replaced by a training requirement for ALLnew and renewing DEA registrants.** Naloxone is an opioid antagonist with poor sublingual bioavailability, and is intended to block buprenorphine's effect only if the tablet is crushed and injected.
Subcutaneous extended-release buprenorphine (monthly)[3,4]	Maintenance	Patients must have received SL buprenorphine-naloxone, 8-2mg daily or higher for at least 1 week. Then-- Month 1: 300 mg x 1. Month 2: If new buprenorphine initiate (has only received for 1-2 weeks), prior daily SL dose was >/+20mg, **or** ongoing cravings or withdrawal give 300 mg x1; otherwise, give 100mg x 1. Month 3 onwards: 100 mg monthly unless clinical indication for higher dose such as ongoing withdrawal symptoms or cravings	As for transmucosal buprenorphine-naloxone, plus injection site reactions	Patients must take at least week of SL buprenorphine formulation at a dose of at least 8-2mg prior to initiating to ensure tolerates	As for transmucosal buprenorphine-naloxone. May be detectable in urine and plasma for 12 mos or more. Weekly and monthly formulations that do NOT require the sublingual trial period first have been developed and studied but not yet available for clinical use.

Buprenorphine implant	Maintenance	Must first be clinically stable on sublingual or buccal buprenorphine at a daily dose of </=8 mg. Then, 12-24 hrs after last transmucosal buprenorphine dose, 4 implants are inserted subdermally by trained clinician in upper arm. Remove within 6 mos after insertion; if continued treatment desired, insert 4 new implants subdermally in contralateral arm. After one insertion in each arm, discontinue treatment implants.	As for transmucosal buprenorphine-naloxone, plus local pain and/or pruritis	Not widely used due to requirement for patients to be on low dose of </=8mg buprenorphine only, and requirement of procedure by specially trained provider	As for transmucosal buprenorphine-naloxone; providers must be specially trained on insertion
Transmucosal buprenorphine	Inpatient withdrawal management; induction; maintenance	For patients with contraindication to naloxone; usual maintenance dose 4mg-24mg sublingually daily.	As for transmucosal buprenorphine-naloxone	Risk of precipitated opioid withdrawal if initiated too soon after last use of full opioid agonist, as above. Periodic monitoring of LFTs is recommended.	As for transmucosal buprenorphine-naloxone.
Intramuscular (IM) naltrexone	Maintenance	380 mg IM every four weeks	Nausea, fatigue, dizziness, injection site reaction.	Risk of precipitated withdrawal if taken < 7 days after last opioid dose (urine drug testing and naloxone challenge may be used to assess risk). Risk of overdose if dose is missed and patient relapses, due to waning opioid tolerance. Periodic monitoring of LFTs is recommended. Impaired metabolism in liver disease.	Some variability in time in days of full opioid blockade reported.
Oral naltrexone	Sometimes given as "bridge" prior to IM naltrexone; can be considered for maintenance in highly	Bridge to IM naltrexone, or maintenance: 25 mg by mouth on day 1, if no withdrawal symptoms occur, start 50 mg daily on day 2	Nausea, headache, dizziness, elevated transaminases	Risk of precipitated withdrawal if taken < 3-6 days after use of short-acting opioids, or <7 days for long-acting opioids. Periodic monitoring of LFTs is recommended. Impaired metabolism in liver disease.	Sometimes used as a bridge treatment to IM naltrexone, to ensure tolerability and/or while awaiting insurance approval. Daily dosing limits effectiveness as a maintenance treatment for opioid dependence.

	supervised settings.				

*This list includes FDA approved medication for alcohol and opioid use disorders. Additional medications are used off-label for alcohol use disorder, with some studies suggesting efficacy, including topiramate, gabapentin, semaglutide and baclofen.

**For details, see: https://www.samhsa.gov/medications-substance-use-disorders/removal-data-waiver-requirement

References

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