

MEDICATIONS USED IN THE MANAGEMENT OF SUBSTANCE USE DISORDERS



Opioid Agonist Therapy (OAT) for Opioid Dependence						
GENERIC (BRAND NAME)	ADULT STARTING DOSE (MAX PER DAY)	ADVANTAGES	DISADVANTAGES	PREGNANCY CATEGORY	SAFETY MARGIN FOR OAT	EFFICACY FOR OAT
Methadone (Dolophine, Methadose)	<ul style="list-style-type: none"> Specialty consultation advised. Titrate carefully, consider methadone's delayed cumulative effects. Individualize dosing regimens (AVOID same fixed dose for all patients). 	<ul style="list-style-type: none"> Give orally in a single daily dose. FDA approved for detoxification treatment and maintenance treatment of Opioid dependence in conjunction with appropriate social and medical services. 	<ul style="list-style-type: none"> Contraindications include any situation where Opioids are contraindicated, such as patients with respiratory depression (in the absence of resuscitative equipment or in unmonitored situations) and patients with acute bronchial asthma or hypercarbia, known or suspected paralytic ileus. May prolong QTc intervals on ECG; risk of cardiac arrhythmias. Discontinue or taper the methadone dose and consider an alternative therapy if the QTc > 500ms. Plasma half-life may be longer than the analgesic duration. Delayed analgesia or toxicity may occur because of drug accumulation after repeated doses, e.g., on days two to five; if patient has excessive sedation during this timeframe, consider temporarily holding dose(s), lowering the dose, and/or slowing the titration rate. 	C/D	<ul style="list-style-type: none"> Serious overdose and death may occur if benzodiazepines, sedatives, tranquilizers, antidepressants, alcohol or other CNS depressants are taken in addition. Methadone contraindicated with selegiline. Avoid concurrent use of methadone with nilotinib, tetrabenazine, ziprasidone, alcohol, st. johns wort, valerian, kava kava, and grapefruit juice. Avoid concurrent use of buprenorphine with alcohol, st. johns wort, valerian and kava kava. 	<ul style="list-style-type: none"> First-line treatment option for chronic Opioid dependence that meets DSM-IV-TR criteria.

Opioid Agonist Therapy (OAT) for Opioid Dependence, Cont.

GENERIC (BRAND NAME)	ADULT STARTING DOSE (MAX PER DAY)	ADVANTAGES	DISADVANTAGES	PREGNANCY CATEGORY	SAFETY MARGIN FOR OAT	EFFICACY FOR OAT
Buprenorphine (Subutex)	<ul style="list-style-type: none"> Specialty consultation advised. Individualize dosing regimens. 	<ul style="list-style-type: none"> FDA approved for management of Opioid dependence. 	<ul style="list-style-type: none"> Major Adverse Effects: hepatitis, hepatic failure, respiratory depression (usually when misused intravenously with other CNS depressants). Common Adverse Effects: headache, pain, abdominal pain, insomnia, nausea, vomiting, sweating, and constipation. Tablets should be placed under tongue until dissolved. Tablets should not be swallowed. Dose should not be started until effects of withdrawal are evident. 	C		
Buprenorphine/Naloxone (Suboxone)	<ul style="list-style-type: none"> Specialty consultation advised. Individualize dosing regimens. 	<ul style="list-style-type: none"> FDA approved for management of Opioid dependence. Combination product recommended for maintenance therapy not initial treatment due to the naloxone. Tablets contain either 2mg buprenorphine /0.5mg naloxone or 8mg buprenorphine/2mg naloxone. Addition of naloxone is intended to decrease the potential for parenteral abuse. 	<ul style="list-style-type: none"> Major Adverse Effects: hepatitis, hepatic failure, respiratory depression (usually when misused intravenously with other CNS depressants). Common Adverse Effects: headache, pain, abdominal pain, insomnia, nausea, vomiting, sweating, and constipation. Tablets should be placed under tongue until dissolved. Tablets should not be swallowed. Drinking warm fluids prior to administration may aid in dissolution. 	C		

Opioid Agonist Therapy (OAT) for Opioid Dependence, Cont.

GENERIC (BRAND NAME)	ADULT STARTING DOSE (MAX PER DAY)	ADVANTAGES	DISADVANTAGES	PREGNANCY CATEGORY	SAFETY MARGIN FOR OAT	EFFICACY FOR OAT
<p>Specialty consultation advised. Methadone or sublingual buprenorphine/naloxone maintenance are first-line therapy due to documented efficacy in improving retention and reducing illicit Opioid use and cravings.</p> <p>Consider appropriate adjustment of Opioid agonist doses to maintain a therapeutic range between signs/symptoms of overmedication (e.g., somnolence, miosis, itching, hypotension, and flushing) and Opioid withdrawal (e.g., drug craving, anxiety, dysphoria, and irritability). Opioid antagonists may precipitate withdrawal. Store in a secure place out of the reach of children. Abrupt cessation may precipitate withdrawal.</p>						
<p>Monitoring, Referrals, and Warnings: Consider baseline ECG and physical examination for methadone patients at risk for QT prolongation or arrhythmias. Perform baseline liver transaminases for buprenorphine or buprenorphine/naloxone therapy. Drug testing for both methadone and buprenorphine should also be considered to ensure compliance with the prescription and for detection of possible diversion. Relapse monitoring to promote effective outcomes. Monitor respiratory status, mental status, and blood pressure.</p> <p>Methadone Black Box Warning: Deaths and life-threatening adverse events, including respiratory depression and cardiac arrhythmias, have occurred upon initiation of treatment for Opioid dependence. Dosage should be selected carefully, titrated slowly and the patient monitored carefully. Use may prolong the QTc interval and increase the risk for torsade de pointes. May cause respiratory depression. For oral administration only. When used for treatment of narcotic addiction, it may only be dispensed by Opioid treatment programs certified by the Substance Abuse Mental Health Services (SAMHSA).</p>						

Opioid Antagonist Therapy for Opioid Dependence

GENERIC (BRAND NAME)	ADULT STARTING DOSE (MAX PER DAY)	ADVANTAGES	DISADVANTAGES	PREGNANCY CATEGORY	SAFETY MARGIN	EFFICACY
Naltrexone (Depade, ReVia)	<ul style="list-style-type: none"> Specialty consultation advised. Extended dosing intervals, using equivalent weekly doses, may be used for supervised administration. 	<ul style="list-style-type: none"> Only the oral formulation of naltrexone is currently FDA-approved for maintenance therapy of Opioid dependence. Side effects, if any, tend to occur early in treatment and can typically resolve within one to two weeks after dosage adjustment. Take with food to minimize nausea especially during the first week. 	<ul style="list-style-type: none"> Contraindications include: acute hepatitis or liver failure, current physiological dependence on Opioids with use within past seven days, ongoing acute Opioid withdrawal or failed naloxone challenge test, receiving Opioid agonists or positive urine Opioid screen. Common Adverse Effects: nausea. No Opioid agonist effects. Patients continue to have cravings and may thereby not be motivated to maintain adherence to the medication regimen. Patients must be fully withdrawn for up to seven to ten days before beginning naltrexone treatment. Precautions include active liver disease, severe hepatic dysfunction, and severe renal failure. Naltrexone is unpopular with many Opioid dependent patients since maintenance therapy requires complete abstinence from Opioids. Treatment dropouts are common. 	C	<ul style="list-style-type: none"> Very large doses of Opioids may overcome the effects of naltrexone and lead to serious injury, coma, or death. Limited clinical experience with over dosage in humans. Drug Interactions include: Opioid-containing medications, including over-the-counter (OTC) preparations, thioridazine, oral hypoglycemic and antiretrovirals. Small doses of Opioids, such as in analgesic, antidiarrheal, or antitussive drugs, may be blocked by naltrexone and fail to produce a therapeutic effect. 	<ul style="list-style-type: none"> FDA approved alternative to Opioid agonist treatment for patients with Opioid dependence. FDA approved for use in alcohol dependency.

Opioid Antagonist Therapy for Opioid Dependence, Cont.

GENERIC (BRAND NAME)	ADULT STARTING DOSE (MAX PER DAY)	ADVANTAGES	DISADVANTAGES	PREGNANCY CATEGORY	SAFETY MARGIN	EFFICACY
<p>Consider Opioid agonist treatment (OAT) or long-term therapeutic community before naltrexone treatment as a first-line approach for chronic Opioid dependent patients. Also, consider engagement in a comprehensive management program that includes measures to ensure medication adherence.</p>						
<p>Monitoring, Referrals, and Warnings: Specialty consultation advised. Baseline evaluation include: naloxone challenge test, transaminase levels and urine toxicology. Therapy is most effective when the patient is engaged in addiction-focused counseling with monitored administration. Repeat transaminase levels monthly for the first three months and every three months thereafter. Discontinue or reduce naltrexone if transaminase levels rise significantly. If signs and symptoms of acute hepatitis occur, discontinue naltrexone and contact provider immediately.</p> <p>Warn patients that attempts to overcome Opioid blockade could lead to fatal overdose. Monitor closely for suicidal thoughts and depression.</p> <p>Black Box Warning: Naltrexone has the capacity to cause hepatocellular injury when given in excessive doses. Patients should be warned of the risk of hepatic injury, advised to stop the use of naltrexone, and seek medical attention if they experience symptoms of acute hepatitis.</p>						

Medication Therapy for Alcohol Dependence (MTAD)

GENERIC (BRAND NAME)	ADULT STARTING DOSE (MAX PER DAY)	ADVANTAGES	DISADVANTAGES	PREGNANCY CATEGORY	SAFETY MARGIN FOR MTAD	EFFICACY FOR MTAD
Naltrexone Oral (Depade, ReVia)	<ul style="list-style-type: none"> Specialty consultation advised. 	<ul style="list-style-type: none"> Side effects, if any, tend to occur early in treatment and can typically resolve within one to two weeks after dosage adjustment. Take with food to minimize nausea especially during the first week of therapy. 	<ul style="list-style-type: none"> Contraindications include receiving Opioid agonists, physiologic Opioid dependence with use within past seven days, acute Opioid withdrawal, failed naloxone challenge test, positive urine Opioid screen, acute hepatitis, or liver failure. Common Adverse Effects: nausea. Need at least three to five days of pretreatment abstinence before starting therapy. Precautions for use in active liver disease or severe renal failure. 	C	<ul style="list-style-type: none"> Very large doses of Opioids may overcome the effects of naltrexone and lead to serious injury, coma, or death. Limited clinical experience with over dosage for naltrexone in humans. Disulfiram contraindicated with metronidazole or ketoconazole therapy, which has already induced a similar reaction to alcohol or hypersensitivity. Drug Interactions for Naltrexone include: Opioid-containing medications, including over-the-counter (OTC) preparations, thioridazine, oral hypoglycemic, and antiretrovirals. Small doses of Opioids, such as in analgesic, antidiarrheal, or antitussive drugs, may be blocked by naltrexone and fail to produce a therapeutic effect. 	<ul style="list-style-type: none"> Naltrexone oral, injectable, acamprosate, and disulfiram FDA approved for use in alcohol dependence. Naltrexone oral is FDA approved for use in Opioid dependency.

Medication Therapy for Alcohol Dependence (MTAD), Cont.

GENERIC (BRAND NAME)	ADULT STARTING DOSE (MAX PER DAY)	ADVANTAGES	DISADVANTAGES	PREGNANCY CATEGORY	SAFETY MARGIN FOR MTAD	EFFICACY FOR MTAD
Naltrexone Inj (Vivitrol)	<ul style="list-style-type: none"> Specialty consultation advised. 	<ul style="list-style-type: none"> Pretreatment abstinence is not required but improves response. Once monthly IM injections. 	<ul style="list-style-type: none"> Contraindications include receiving Opioid agonists, physiologic Opioid dependence with use within past seven days, acute Opioid withdrawal, failed naloxone challenge, positive urine Opioid screen, acute hepatitis, or liver failure or inadequate muscle mass. Major Adverse Effects: Eosinophilic pneumonia, depression, and suicidality. Common Adverse Effects: Injection-site reactions, nausea, headache, and asthenic conditions. Discontinue IM Naltrexone if there is NO detectable benefit within three months. Precautions for use in active liver disease or moderate to severe renal insufficiency. Potential injection site reactions. 	C	<ul style="list-style-type: none"> Avoid concurrent use of disulfiram with alcohol in food such as sauces, vinegars or beverages, and medications such as cough syrups. Avoid disulfiram if alcohol intoxicated. 	
Acamprosate (Campral)	<ul style="list-style-type: none"> Specialty consultation advised. 	<ul style="list-style-type: none"> Tablets should be swallowed whole, do not chew or crush. May be taken without regard to meals; however, administration with meals may improve compliance. 	<ul style="list-style-type: none"> Contraindications include severe renal impairment ($\text{CrCl} \leq 30 \text{ mL/min}$). Major Adverse Effects: suicidality. Common Adverse Effects: diarrhea. Abstinence at treatment initiation and during treatment. Do not administer to patients with severe renal impairment. 	C		

Medication Therapy for Alcohol Dependence (MTAD), Cont.

GENERIC (BRAND NAME)	ADULT STARTING DOSE (MAX PER DAY)	ADVANTAGES	DISADVANTAGES	PREGNANCY CATEGORY	SAFETY MARGIN FOR MTAD	EFFICACY FOR MTAD
Disulfiram (Antabuse)	<ul style="list-style-type: none"> Specialty consultation advised. 	<ul style="list-style-type: none"> Can be used also in alcohol dependence combined with cocaine. Can be used with failure of or contraindication to naltrexone therapy. Used in one who has the capacity to appreciate risks and benefits and to consent to treatment. More effective with monitored administration (e.g., in clinic, with spouse, or probation officer). 	<ul style="list-style-type: none"> Contraindications include severe cardiovascular, respiratory, or renal disease, severe hepatic dysfunction (i.e., transaminase levels > three times upper limit of normal or abnormal bilirubin), severe psychiatric disorders, especially psychotic and cognitive disorders and suicidal ideation, and/or poor impulse control. Major Adverse Effects: hepatotoxicity, peripheral neuropathy, psychosis, delirium, severe disulfiram ethanol reaction. Common Adverse Effects: somnolence, metallic taste, and headache. Abstinence > 24 hours and BAL equal to 0. 	C		
<p>Success is enhanced by engagement in a comprehensive management program that includes psychosocial therapy. Naltrexone IM or acamprostate should be routinely considered when treating alcohol dependence with addiction counseling. Disulfiram should only be used when abstinence is the goal. Compliance improves when disulfiram administration is directly observed. Inform the patient to use caution when operating vehicles and hazardous machinery since disulfiram may cause sedation.</p>						

Monitoring, Referrals and Warnings: Naltrexone Oral and IM baseline evaluation include liver transaminase, bilirubin and urine beta-HCG for females. Naltrexone IM also should have baseline CR levels drawn. Repeat naltrexone liver transaminase levels at six and 12 months and then every 12 months thereafter. Naltrexone IM may cause allergic pneumonia, monitor appropriately. Monitor for signs and symptoms of acute hepatitis, discontinue naltrexone if signs appear and contact provider immediately. Patients who have previously used Opioids may be more sensitive to toxic effects of Opioids after discontinuation of naltrexone.

If the patient consumes alcohol with disulfiram then a disulfiram-alcohol reaction will occur and may persist for 30 minutes to several hours afterwards. Reaction can include flushing, throbbing in the head or neck, nausea, vomiting, sweating, chest pain, palpitation, tachycardia, hypotension, syncope, weakness, vertigo, blurred vision, and confusion. Severe reactions include respiratory depression, cardiovascular collapse, arrhythmias, MI, convulsions, and death. Warn patients accordingly. Family members should not administer disulfiram without informing the patient. Provide patients with wallet cards that indicate the use of disulfiram.

Monitor closely for suicidal thoughts and depression.

Black Box Warning: Naltrexone has the capacity to cause hepatocellular injury when given in excessive doses. Patients should be warned of the risk of hepatic injury and advised to stop the use of naltrexone and seek medical attention if they experience symptoms of acute hepatitis.

Disulfiram should never be administered to a patient when the patient is in a state of alcohol intoxication or without his/her full knowledge. Advise the relatives that disulfiram should not be used to treat alcohol intoxication.