Treatment of Substance Use Disorders

Pharmacotherapy for Nicotine Dependence[1]

Nicotine Replacement Therapy (NRT)[2,3]				
Type	**Instructions and dosing**	**Side effects/concerns**	**Formulary Status with HPSM**	**Comments**
Patch (OTC & R_x)	>10 cigarettes/d: 21 mg/d (step 1) for 6 weeks followed by 14 mg/d (step 2) for 2 weeks; finish with 7 mg/d (step 3) for 2 weeks ≤10 cigarettes/d: 14 mg/d (step 2) for 6 weeks followed by 7 mg/d (step 3) for 2 weeks ▪ individualize based on pt characteristics (previous patch experience, amount smoked, degree of dependence, experiencing WDL or AEs) ▪ treatment of ≤ 8 weeks has been shown as efficacious as longer treatment	▪insomnia &/or vivid dreams ▪ local skin reaction usually self-limiting, hydrocortisone 1% or triamcinolone 0.5% cream & rotating patch sites may help (require discontinuation of patch in <5% pts)	Formulary with quantity limits	▪ Effective, 1st line agent (strength of evidence: A) ▪ continuous nicotine delivery, require 6-8 hrs to achieve peak serum concentrations ▪ delivers nicotine to the CNS more slowly than any other NRT ▪ apply on the quit day as soon as pt wakes up ▪ remove the 24-hr patch prior to bedtime or use 16-hr patch in case of sleep disruption ▪ data shows that patch use almost doubles the likelihood of long-term abstinence compared to placebo ▪ no pediatric dosing guidelines
Gum (OTC)	2 mg: smoking < 25 cigarettes/d 4 mg: ≥25 cigarettes/d ▪ every 1 to 2 hrs for the first 6 weeks, may be used for up to 12 weeks ▪ Max: 24 pieces a day ▪ Chew slowly until peppery/flavored taste is noted. Then "park" between cheek & gum to facilitate absorption until the tingling is almost gone. Repeat for about 30 min ▪ Avoid beverages other than water 15 min before or during (pH changes affect absorption)	mouth soreness, hiccups, dyspepsia, & jaw ache (mild & transient, improved by correcting the chewing technique) CI: use in temporomandibular joint disease	Formulary with quantity limits	▪ Effective, 1st line med (strength of evidence: A) ▪ offer 4 mg to highly dependent smokers ▪ data demonstrates that gum use increased the likelihood of long-term abstinence by ~50 % compared to placebo ▪ no pediatric dosing guidelines
Lozenge (OTC)	2 mg: smoke 1st cigarette > 30 min after waking 4 mg: smoke 1st cigarette within 30 min of waking	▪ mouth irritation, heartburn, hiccups, & nausea ▪ HA & coughing (4 mg dose)	Formulary with quantity limits	▪ Effective, 1st line med (strength of evidence: B) ▪ no pediatric dosing guidelines

	▪ Max 5 lozenges in 6 hours or 20 lozenges/d ▪ clts often do not use enough prn NRT to gain optimal effects. Generally, smokers should use 1 lozenge Q 1 to 2 hrs first 6 weeks, Q 2-4 hrs during weeks 7-9, followed by Q 4–8 hrs during weeks 10-12 ▪ must be sucked (vs bitten or chewed) ▪ taper over 6-12 weeks (can be longer)	▪ eating or drinking beverages other than water immediately before or during using a gum or lozenge should be avoided (pH changes can blunt nicotine absorption)		
Nasal Spray (R_x)	▪ one 0.5 mg dose administered via each nostril (total 1 mg) ▪ initial: 1 to 2 doses/hr, increasing freq to prn symptom relief ▪ administer with the head tilted slightly back ▪ do not sniff, swallow, or inhale through the nose during administration to minimize irritating effects ▪ minimum: 8 doses/d, max: 40 doses/d (5 doses/hr) ▪ 100 doses per bottle ▪ duration of therapy: 3 to 6 months	▪ nasal & throat irritation, rhinitis, sneezing, coughing, watery eyes, flushing, nasal congestion, transient changes in sense of smell & taste ▪ AEs common cause of discontinuation ▪ avoid use in clts with severe reactive airway disease	Nonformulary	▪ Effective, 1st line agent (strength of evidence: A) ▪ highest dependence potential (higher peak nicotine levels compared to other NRTs) ▪ avoid use in individuals with other SUDs that involve snorting (reinforces the behavior) ▪ fastest-acting (but much slower than cigarettes), faster relief of nicotine withdrawal symptoms (T_{max}: 4-15 min) ▪ no pediatric dosing guidelines
Inhaler (R_x)	Dose: 6 to 16 cartridges a day ▪ nicotine cartridge placed inside hollow cigarette like plastic rods, produce nicotine vapor ▪ each cartridge delivers 4 mg nicotine over 80 inhalations ▪ best effects attained by frequent inhalation & using ≥ 6 cartridges/d ▪ avoid beverages other than water 15 min before or during inhaler use (pH changes affect absorption) ▪ duration of therapy: up to 6 months, taper during the last 6-12 weeks	▪ mouth & throat irritation, cough & rhinitis ▪ frequency of symptoms declined with continued use ▪ tolerance usually develops within 1-2 days	Nonformulary	▪ Effective, 1st line agent (strength of evidence: A) ▪ Facilitates/reinforces hand to mouth behaviors of smoking ▪ not a true pulmonary inhaler, nicotine absorbed across oropharynx mucosa ▪ data shows that inhaler use almost doubles the likelihood of long-term abstinence compared to placebo ▪ nicotine delivery declines significantly at T <40°F. Keep inhaler & cartridges in an inside pocket or other warm area in cold weather ▪ no pediatric dosing guidelines

Other Medications for Nicotine Dependence

Medication	Mechanism of Action	Dosage & Administration	Adverse Effects	Formulary Considerations	Comments
Buproprion SR (Zyban)	Dopamine & NE reuptake inhibitor, some nicotinic acetylcholinergic receptor blocking activity	Initial: 150 mg QAM Max: 300 mg/d ▪ begin treatment 1–2 weeks prior to quit date to allow steady state serum concentrations ▪ Duration of treatment: up to 6 months for long-term therapy	insomnia, dry mouth, HA, jitteriness, agitation, nausea & constipation ▪ CIs: h/o seizures or eating disorders, clts on another form of bupropion, MAOI use in the past 14 days ▪ clts with conditions that increase seizure risk such as arteriovenous malformation, severe head injury, stroke, brain tumor, CNS infection should not take bupropion	Formulary	▪ Effective, 1st line med (strength of evidence: A) ▪ as effective as single NRT in increasing ≥6 months smoking cessation rates & reducing weight gain ▪ FDA approved since 1997 ▪ taking PM dose earlier (≥ 8 hrs after AM dose) may help with insomnia ▪ option to use in combination with NRTs ▪ limited data available for use in adolescents ≥14 yrs & ≥40.5 kg; shown to be effective short-term in 104 adolescents treated for 7 weeks with cessation counseling ▪ Pregnancy: limited human data suggest low risk
Varenicline (Chantix)	Selective partial agonist activity at $\alpha_4\beta_2$ neuronal nicotinic acetylcholine receptors (mediates dopamine release relieving cravings/withdrawal sx), competitively blocks exogenous nicotine binding Higher affinity for α4β2 receptor vs. nicotine → reduced reward associated with smoking	▪ Target: 1 mg BID ▪ Renal dose adjustment needed for CrCl < 30 ml/min ▪ Start 1 week prior to quit date to allow steady state concentrations ▪ Starter pack available ▪ Take after eating with a full glass of water	▪ N/V, abnormal dreams, HA, sleep disturbances, constipation & flatulence ▪ Neuropsychiatric sx, exacerbations of pre-existing psychiatric disorders, suicidal thoughts, & increased rate of CV events ▪ Data from a retrospective study (n ~ 165,000) suggests varenicline was not associated with an increased risk of any CV or neuropsychiatric event compared to NRT or bupropion	Formulary with quantity limits	▪ Data including long-term trials up to 1 yr indicates varenicline to be more effective than single NRT or bupropion and as effective as combination NRT in improving smoking cessation rates ▪ data also shows increased smoking cessation rates in pts with psych disorders without causing significant neuropsychiatric AEs ▪ a double-blind comparative trial (n=8144) found varenicline to be the most effective treatment, whereas bupropion & nicotine patch were similar in efficacy ▪ FDA approved in ages ≥17 yo, did not demonstrate efficacy for ≤16 yo

					▪ no clinically significant DDIs ▪ Pregnancy: limited human data, animal data suggest low risk

ELECTRONIC NICOTINE DELIVERY SYSTEMS: Electronic or e-cigarettes are not FDA approved as smoking cessation aids. They are advertised as a safer, convenient & socially acceptable substitute to tobacco cigarettes. According to the CDC as of October 15, 2019; 1,479 cases of lung injury have been reported and 33 deaths have been confirmed with e-cigarette/vaping products use. No consistent evidence of infectious disease has been identified indicating that the lung injuries are likely associated with chemical exposure. Most patients reported a h/o tetrahydrocannabinol (THC) containing products use.

Combination Strategies

Nicotine Patch plus	Gum
	Lozenge
	Inhaler
	Spray
Bupropion SR plus	Patch
	Gum
	Lozenge
Varenicline Plus	Gum
	Lozenge
	Inhaler
	Spray

1: please refer to Table A regarding effectiveness & abstinence rates. First-line medications are listed by size of the odds ratio; **2**: reduces the severity of nicotine withdrawal symptoms. Not an independent risk factor for acute myocardial events, use with caution in cardiovascular pts (within 2 weeks post MI, serious arrhythmias, & unstable angina pectoris); **3**: NRT Pregnancy Recommendation (Briggs Drugs in Pregnancy and Lactation): Compatible if maternal Benefit >> embryo/fetal risk. Contraindicated with any tobacco use. Non-pharmacologic approaches are the safest option, but if failed, NRT use during pregnancy might be reasonable. Pt education must include that if they continue to smoke while using NRT, the embryo/fetus risk might be greater than when either is used alone. Breast-feeding Recommendation: No human data, potential toxicity
Strength of evidence: - **A**: Multiple well-designed randomized clinical trials, directly relevant to the recommendation, yielded a consistent pattern of findings; **B**: Some evidence from randomized clinical trials supported the recommendation, but the scientific support was not optimal. For instance, few randomized trials existed, the trials that did exist were somewhat inconsistent, or the trials were not directly relevant to the recommendation; **C**: Reserved for important clinical situations in which the Panel achieved consensus on the recommendation in the absence of relevant randomized controlled trials

Pharmacotherapy for Alcohol-Related Disorders

Medication / Class	MOA	Dose & Administration	Adverse Effects Contra-indications & Monitoring	Formulary Considerations	Comments
Naltrexone (ReVia) Full antagonist	▪ μ opioid antagonist similar in structure to naloxone ▪ acts as a competitive antagonist & effectively blocks opioid receptors ▪ may block the pleasurable effects of alcohol mediated release of endogenous opioids	▪ 50 mg PO daily ▪ Some clts may require up to 100 mg/d	▪ nausea, headache, anxiety, sedation ▪ warnings of hepatotoxicity are derived from studies using dose up to 350mg/d for obesity & dementia. No reports of hepatotoxicity at 50 mg/d ▪ Liver enzymes in alcoholic pts tend to improve with naltrexone likely due to reduced alcohol consumption CIs: opioid dependence or current use of opioids, acute opioid WDL; failure to pass naloxone challenge or positive urine screen Monitor for opioid WDL, LFTs**, INR prior to initiation, depression and/or suicidal thinking	Formulary	▪ One of the best studied & underutilized treatments for alcohol dependence. Studies favor a reduction in heavy drinking over complete abstinence ▪ pts must be opioid free for 7-10 days (depending on half-life of opioids used) before starting naltrexone as determined by urinalysis. Consider naloxone challenge test, if any suspicion ▪ contraindicated in opioid dependent clts or pts receiving chronic treatment with opioids for pain or addiction treatment ▪ some studies have shown efficacy when combined with acamprosate ▪ no pediatric dosing guidelines Prescribing Dispensing Restrictions ▪ any individual licensed to prescribe medicines ▪ any pharmacy can fill the Rx
Naltrexone ER injection (Vivitrol) Full antagonist		380 mg monthly IM inj administered by a qualified staff	▪ hepatic enzyme abnormalities, injection site pain, nasopharyngitis, insomnia, & toothache ▪ vulnerability to opioid overdose ▪ CIs: opioid dependence or current use of opioids, undergoing opioid withdrawal, failure to pass naloxone challenge or positive urine screen, body mass precludes IM inj (SQ inj may cause severe inj site reaction) Monitor for opioid WDL, LFTs**, INR prior to initiation, inj site reactions, depression & /or suicidal thinking	Formulary, carved out to State MediCal	▪ ideal for *motivated* clts experiencing relapse risks or being treated for co-occurring OUD, with strong psychosocial support, less severe addiction history, unable to or undecided regarding agonist treatment ▪ Pros: established efficacy, once monthly inj may improve adherence, fixed dose, non-addictive, reduces rewarding effects of opioids/alcohol ▪ Cons: require initial abstinence, little effect on opioid cravings, may precipitate addiction relapse, poor pt adherence, r/o overdose in clts concurrently using opioids ▪ For clts who can abstain from alcohol in an outpatient setting prior to treatment initiation, not shown to be effective in clts drinking at treatment initiation

					▪ may cause false positive on some urine drug tests (specifically opioids) ▪ no pediatric dosing guidelines
Acamprosate (Campral)	Structurally similar to GABA appears to increase GABA-ergic & ↓ glutamate activity in the CNS including reduced NMDA receptors activity	666mg TID lower dose may be effective in some pts ▪ CrCl 30-50 **ml/min: initial dose 333mg TID ▪ Cl_{Cr} <30ml/min: contraindicated	Diarrhea, insomnia, anorexia, weakness, anxiety, depression, & suicidality CI: Severe renal impairment Monitor for alcohol abstinence, depression, suicidal thinking, & renal function	Formulary, carved out to State MediCal	▪ pill burden (TID dosing) ▪ comparative studies show inferiority to naltrexone. Some studies show efficacy when combined with naltrexone ▪ safe in liver disease ▪ reduces alcohol intake w/o causing disulfiram-like reaction following alcohol ingestion ▪ initiate treatment as soon as possible following alcohol withdrawal when pt has achieved abstinence (continue if pt relapses) ▪ no pediatric dosing guidelines
Topiramate (Topamax)	Blocks voltage dependent Na+ channels, augments GABA-A activity, antagonizes AMPA/kainate subtype glutamate receptors, & weakly inhibits carbonic anhydrase	Initial: 50 mg QHS, titrate up to 150 mg BID ▪ Renal dose adjustment needed for CrCl <70 ml/min	paresthesia, fatigue, drowsiness, dizziness, memory impairment, ↓ serum bicarb, hyperammonemia, abdominal pain, anorexia, weight loss, altered sense of taste, nausea, diarrhea, infection, fever, flushing, impaired concentration, depression, insomnia, mood disorder, hypoesthesia, anxiety, cognitive dysfunction, psychomotor impairment, dyspepsia, hemorrhage, arthralgia, conjunctivitis, sinusitis, cough, rhinitis, pharyngitis, bronchitis, accidental injury, language problems	Formulary	▪ moderate quality evidence favors significant reduction in heavy drinking & promotion of abstinence ▪ shown to be at least as effective as naltrexone in head to head trials ▪ consider as 1st line therapy in pts with co-occurring seizure disorder ▪ reduces alcohol craving through glutamate antagonism & inhibition of dopamine release ▪ some AEs managed by reducing dose ▪ 200 mg /d has been shown to be effective & less likely to cause AEs ▪ monitor electrolytes, sCr, hydration status, sx of acidosis, ammonia lvl in pts with unexplained lethargy, vomiting, mental status changes, IOP, sx of secondary angle closure glaucoma, suicidality, eating behaviors, & sedation ▪ pediatric dosing available for use as an anticonvulsant, treatment of infantile spasms, & migraine px
Gabapentin (Neurontin)	Structurally similar to GABA but does not bind to GABA receptors. Binds to $alpha_2delta_1$ subunit of voltage gated	Initial: 300 mg/d ▪ titrate up to 300-600 mg/d ▪ renal dose adjustment	sedation, dizziness, ataxia, fatigue, peripheral edema, hostility, emotional lability, N/V, diarrhea, xerostomia, infection, tremor, asthenia, hyperkinesia, nystagmus, &	Formulary	▪ Studies indicate higher rates of abstinence & lower rates of heavy drinking compared to placebo ▪ alternative when 1^{st}-line agents cannot be used ▪ potential for misuse by some pts with SUD

	calcium channel modulating release of excitatory NTs	needed for CrCl <60 ml/min	diplopia		▪ Monitoring: periodic renal fn, suicidality, and signs of addiction & dependence ▪ pediatric dosing available for the treatment of neuropathic pain & seizures
Disulfiram (Antabuse)	Irreversibly inhibits acetaldehyde dehydrogenase which results in accumulation of acetaldehyde when alcohol is consumed producing flushing, throbbing in head & neck, N/V, diaphoresis, thirst, chest pain, syncope, vertigo, tachycardia, SOB, confusion & hypotension	▪ Initial: 250mg/d at least 12 hr after last drink ▪ Range: 125 to 500 mg/d ▪ AM administration preferred when the desire to abstain is greatest ▪ may be given qhs d/t sedation	idiosyncratic dose-independent hepatotoxicity, optic neuritis, neuropathies, metallic aftertaste, impotence, psychosis, drowsiness, fatigue, & HA CIs: clts using alcohol, metronidazole, paraldehyde, or alcohol-containing preparations, psychosis, severe myocardial dz or coronary occlusion ▪ Monitoring: Baseline LFTs & after 10-14 days of treatment	Formulary, carved out to State MediCal	▪ aversive agent to discourage pts from using alcohol due to AEs of acetaldehyde accumulation ▪ do not use in pts unable to abstain or understand severity of alcohol-disulfiram reaction d/t medical risks ▪ supervised administration is best ▪ limited effectiveness in blinded trials since pts on placebo may still be dissuaded from drinking d/t potential aversive effects ▪ avoid all exposure to alcohol including sauces, aftershave lotion, mouthwashes, & cough meds. Effects can last up to 14 days ▪ no pediatric dosing guidelines

Pharmacotherapy for Opioid-Related Disorders

Medication / Class	MOA	Dosage & Administration	Adverse Effects	Formulary Considerations	Prescribing Dispensing Restrictions	Comments
Buprenorphine ER injection (Sublocade®) ▪Partial agonist/antagonist ▪ Schedule III	▪ partial μ receptor agonist & κ receptor antagonist ▪ BUP's analgesic effects plateau at higher doses & it then acts as an antagonist	▪ 2 initial doses of 300mg SQ monthly ▪ maintenance dose: 100 to 300 mg monthly ▪ administered in the abdominal region by a healthcare provider in a health care setting	constipation, headache, nausea, injection site pruritus/pain, vomiting, increased hepatic enzymes, & fatigue	Formulary, carved out to State MediCal	available through Sublocade REMS program only	▪ treatment of moderate to severe OUD for clts initiated & taking transmucosal BUP containing product for at least 1 week ▪ not recommended in moderate to severe hepatic impairment ▪ BB: risk of serious harm/death if given IV ▪ may reduce non-adherence & diversion ▪ appears to be at least as effective as methadone in reducing mortality ▪ unlikely to prolong QT interval ▪ expensive, not compared with other meds ▪ use with other CNS depressants may lead to drowsiness/overdose ▪ ceiling on respiratory depressant effect →

						lower r/o abuse/overdose ▪ to be used in conjunction with counseling & psychosocial support ▪ adolescent dosing guidelines available for buprenorphine and naloxone. ▪ safety & effectiveness of Sublocade have not been established in pediatric pts
Methadone ▪ Full agonist ▪ Schedule II	Full μ opioid agonist with 24 hrs half-life	▪ no single dose is optimal for all clts ▪ some pts may require > 100 mg/d ▪ heroin addicts with psychiatric co-morbidities generally require higher doses ▪ taken once daily orally, usually witnessed at an OTP until clt receives take-home doses ▪ no pediatric dosing guidelines	constipation, some cognitive effects, r/o QTc prolongation, lightheadedness, dizziness, sedation, N/V, sweating, weakness, abdominal pain, reduced libido, visual disturbances, arrhythmias ▪ overdose produces respiratory depression & death	Formulary	▪ available through specially licensed opioid treatment programs only ▪ DEA registered licensed MD who works at an OTP ▪ Dispensed only at certified OTPs or hospitals*	▪ to alleviate cravings & withdrawal symptoms ▪ goal is to achieve stable maintenance dose & facilitate clt engagement in a comprehensive program ▪ Pros: established efficacy, long history of use (~50 yrs), detoxification & maintenance treatment for motivated clts ▪ Cons: taken daily, require frequent visits to OTPs, high abuse/diversion potential ▪ pediatric dosing guidelines available for the treatment of iatrogenic opioid dependency (limited data)
Buprenorphine-Naloxone (Suboxone® - Zubsolv®) ▪ Partial agonist/antagonist ▪Schedule III	▪ mixed opioid agonist-antagonist ▪ buprenorphine - partial μ receptor agonist & κ receptor antagonist ▪ naloxone - μ opioid antagonist	▪ SL film ▪ Initiation via induction - individual must be in moderate WDL from all opioids ▪ Dose: 8-2 to 32-8 mg once daily ▪ No pediatric dosing guidelines	headache, insomnia, sweating, constipation, nausea, pain, vasodilation, potential liver complications ▪ film: glossodynia, oral hypoesthesia & oral mucosa erythema	Formulary with quantity limits, carved out to State MediCal	▪ DEA registered licensed MD who either works at an OTP or have a waiver to prescribe BUP ▪ any pharmacy can fill ▪ may be taken at physician's office or at home	▪ caution when prescribing with benzos – fatalities have been reported, mainly when both are taken parenterally ▪ to alleviate cravings & WDL symptoms ▪ Pros: established efficacy, may prescribe for up to a month, avoidance of specialty clinics & reduced abuse potential, overdose does NOT produce significant respiratory depression ▪ Cons: taken daily, some abuse potential, may precipitate WDL if initiated before clt is in opioid WDL particularly clts being transferred from methadone, MDs need limited special training

New Dosage Strength (Cassipa)	▪ naloxone added to reduce diversion				▪ prescribed by Drug Addiction Treatment Act certified prescribers	▪ adolescent dosing guidelines available for buprenorphine and naloxone
		▪ 16mg/4mg SL film given as a single daily dose ▪ co-administration of liquids ↓ BUP & naloxone systemic exposure up to 59 & 76% respectively depending on liquid pH ▪ dosage adjustments may be necessary when switched from tablets to film or vice-versa	reduced sense of oral sensation, inflammation of oral mucosa, headache, N/V, excessive sweating, constipation, S/Sx of withdrawal, insomnia, pain, & peripheral edema	Nonformulary		▪ to be used after induction & stabilization to 16 mg BUP dose in conjunction with counseling & psychosocial support ▪ not recommended in severe hepatic impairment ▪ reduces cravings/WDL sx without producing the same euphoria as methadone ▪ partial μ-opioid agonist → less potential for abuse, lower r/o overdose ▪ relatively safe for take-home dosing ▪ ceiling effect for respiratory depression ▪ unlikely to prolong QT interval ▪ does not appear to retain individuals in treatment as well as methadone ▪ studies indicate that BUP works better at higher daily doses (≥16mg) ▪ safety & effectiveness have not been established in pediatric pts
Naltrexone (ReVia) **Naltrexone ER injection (Vivitrol)**	▪ μ opioid antagonist similar in structure to naloxone ▪ acts as a competitive antagonist & effectively blocks opioid receptors ▪ may block the pleasurable effects of alcohol mediated release of endogenous opioids	▪ Oral: Start at 25mg/d for 7 days to improve tolerability ▪ target dose: 50mg/d ▪ can be given 3 times a week: 100 mg on Mon, Wed & 150 mg on Friday ▪ Inj: 380mg IM monthly	nausea, headache, anxiety, sedation ▪ Warnings of hepatotoxic effects are derived from studies using dosages up to 350mg/d for obesity & dementia ▪ no reports of hepatotoxicity at recommended daily dose of 50mg ▪ liver enzymes in alcoholic pts tend to improve with naltrexone likely due to reduced	Formulary, Carved out to State MediCal Formulary, Carved out to State MediCal		▪ mixed efficacy for opioid dependence ▪ positive results in inpatient studies ▪ higher dropout rates with outpatient studies likely related in part to the absence of a psychoactive effect ▪ most effective in *motivated* individuals ▪ clients must be opioid free for 7-10 days before starting naltrexone ▪ naltrexone ER IM for clts detoxified from opioids (fully withdrawn for at least 7 days, 14 days for methadone & BUP) in conjunction with counseling & psychosocial support ▪ ER inj minimize opportunities for non-adherence, produces more consistent/predictable drug concentration (depot inj bypasses 1st pass metabolism) ▪ Cons: require initial abstinence, little effect on opioid cravings, may precipitate addiction

			alcohol consumption			relapse, poor pt adherence, r/o overdose in clts concurrently using opioids ▪ no pediatric dosing guidelines

AUD: alcohol use disorder, BB: black box warning, BSL: baseline, BUP: buprenorphine, CIs: contraindications, DNE: do not exceed, Dz: disease, ER: extended-release, HA: headache, inj: injection, MOA: mechanism of action, NE: norepinephrine, NT: neurotransmitter, OTPs - opioid treatment programs, OUD: opioid use disorder, px: prophylaxis, r/o: risk of, SL: sublingual, WDL – withdrawal, W/O: without, *for opioid dependence treatment purposes, 1: APA alcohol use disorder guidelines recommend that acamprosate should not be used 1st line for pts with mild to moderate renal impairment

**https://pcssnow.org/wp-content/uploads/2014/10/PCSS-MAT-NTX-Liver-Safety-Guideline1.pdf

Table A: Meta-analysis (2008): Effectiveness and abstinence rates for various medications and medication combinations compared to placebo at 6-months post quit (n = 83 studies)[*#]

Medication	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
Placebo	80	1.0	13.8
Monotherapies			
Varenicline (2 mg/day)	5	3.1 (2.5–3.8)	33.2 (28.9–37.8)
Nicotine Nasal Spray	4	2.3 (1.7–3.0)	26.7 (21.5–32.7)
High-Dose Nicotine Patch (> 25 mg) (These included both standard or long-term duration)	4	2.3 (1.7–3.0)	26.5 (21.3–32.5)
Long-Term Nicotine Gum (> 14 weeks)	6	2.2 (1.5–3.2)	26.1 (19.7–33.6)
Varenicline (1 mg/day)	3	2.1 (1.5–3.0)	25.4 (19.6–32.2)
Nicotine Inhaler	6	2.1 (1.5–2.9)	24.8 (19.1–31.6)
Clonidine	3	2.1 (1.2–3.7)	25.0 (15.7–37.3)
Bupropion SR	26	2.0 (1.8–2.2)	24.2 (22.2–26.4)
Nicotine Patch (6–14 weeks)	32	1.9 (1.7–2.2)	23.4 (21.3–25.8)
Long-Term Nicotine Patch (> 14 weeks)	10	1.9 (1.7–2.3)	23.7 (21.0–26.6)
Nortriptyline	5	1.8 (1.3–2.6)	22.5 (16.8–29.4)
Nicotine Gum (6–14 weeks)	15	1.5 (1.2–1.7)	19.0 (16.5–21.9)
Combination therapies			
Patch (long-term; > 14 weeks) + *ad lib* NRT (gum or spray)	3	3.6 (2.5–5.2)	36.5 (28.6–45.3)
Patch + Bupropion SR	3	2.5 (1.9–3.4)	28.9 (23.5–35.1)
Patch + Nortriptyline	2	2.3 (1.3–4.2)	27.3 (17.2–40.4)
Patch + Inhaler	2	2.2 (1.3– 3.6)	25.8 (17.4–36.5)
Patch + Second generation antidepressants (paroxetine, venlafaxine)	3	2.0 (1.2–3.4)	24.3 (16.1–35.0)

Medications not shown to be effective			
Selective Serotonin Re-uptake Inhibitors (SSRIs)	3	1.0 (0.7–1.4)	13.7 (10.2–18.0)
Naltrexone	2	0.5 (0.2–1.2)	7.3 (3.1–16.2)

*# Go to www.surgeongeneral.gov/tobacco/gdlnrefs.htm for the articles used in this meta-analysis.

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