



City and County of San
Francisco
Daniel Lurie
Mayor

**San Francisco Health Network Behavioral Health Services
Medication Use Improvement Committee**
1380 Howard St. 5th Floor
San Francisco, CA 94103



MEDICATIONS FOR NICOTINE USE DISORDERS TREATMENT GUIDELINE

SCOPE: This Medications for Nicotine Use Disorders (MNUD) Treatment Guideline is intended to offer information for providers, clients and the interested public to increase the utilization and effectiveness of MNUD. It is not intended to be comprehensive in scope. These recommendations are not a substitute for clinical judgment, and decisions about care must carefully consider and incorporate the clinical characteristics and circumstances of each individual client.

INTRODUCTION: NUD are chronic, remitting and relapsing diseases characterized by the compulsive use of tobacco and/or other nicotine products despite known negative health and psychosocial consequences. As with many substances with misuse potential, the DSM-5-TR details diagnostic criteria for Tobacco Use Disorder (TUD; specifiers: in early remission, in sustained remission, on maintenance therapy, in a controlled environment, mild, moderate, severe) in addition to Tobacco Withdrawal, and Unspecified Tobacco-Related Disorder. To meet criteria for TUD, clients must exhibit at least 2 out of 11 DSM-5-TR criteria over a 12-month period leading to clinically significant impairment and/or distress. The severity of the use disorder is based on the number of criteria met with mild use disorder associated with 2-3, moderate use disorder associated with 4-5, and severe use disorder associated with 6 or more criteria met. Frequency of nicotine use as well as earlier age of use onset are associated with higher severity NUD. While the broader term NUD is not used in the DSM5-TR, we are employing it here to acknowledge the increasing importance of also treating non-tobacco-related nicotine use (e.g. electronic cigarettes [e-cigarettes]).

The disease burden from nicotine products can arguably be conceptualized on a relative risk scale. Combustible tobacco products (e.g. cigarettes, cut tobacco, bidis, cigarillos, water pipe tobacco, western pipe tobacco, smokeless tobacco, and cigars) occupy the highest risk category. Orally delivered tobacco products (e.g. chewing tobacco, dip tobacco, snus) are in a moderately lower risk category. E-cigarettes and heat-not-burn devices occupy a mildly lower risk category. Finally, traditional NRT (e.g. nicotine gums, lozenges, patches) is the second lowest risk category next to not using nicotine at all. From a harm reduction perspective, one goal may be to help those with NUD move from higher risk category use to lower risk category use and ideally abstinence. Clinical professional organizations' expert opinions, recommendations, and guidelines will likely be changing in the face of increasing publications of randomized control trials (RCTs) on non-combustible NUD treatments.

In the past 60 years smoking rates have significantly declined from approximately 40% prevalence in 1965 to 11.6% in 2022. The use of e-cigarettes and other electronic nicotine delivery systems has remained somewhat stable in adults over the last 20 years with a recent increase from 4.5% in 2021 to 6% in 2022. Rates of e-cigarette use in middle and high schoolers increased steadily from 2011 to a peak in 2019 of 27.5% and decreased to 5.9% in 2024. Smoking rates have also decreased in people with mental health (MH) and/or substance use disorders (SUD) and these populations still experience double the rates of NUD. Nearly half of all deaths occurring in those being treated for SUD and/or severe MH disorders are due to tobacco-related illnesses and tobacco-related deaths occur decades earlier than in the general population. Most people with SUD and MH disorders want to quit using nicotine products and want

information and resources to aid in so doing and are in many cases willing and ready to attempt to quit using nicotine products.

Challenges to NUD treatment in the SUD and MH populations include a history of tobacco used as a therapeutic tool in treatment facility settings, lack of adequate staff training, lack of knowledge about treatment resources, and time constraints. Providers and clients alike may share concerns about MH or SUD symptom relapse/exacerbation. On the contrary, persons who abstain from tobacco use during SUD treatment are less likely to relapse to other drugs or alcohol. Although it is not uncommon for people to believe that nicotine helps improve or control MH symptoms, research suggests that nicotine use is associated with greater depressive symptoms, anxiety and an increase in suicidal behavior. People with depression, schizophrenia and post-traumatic stress disorder can quit without impairing their mental health recovery. Having a psychiatric disorder can make this population more susceptible to relapses related to stress and other emotional drivers. In fact, a psychiatric diagnosis is a risk factor for relapse even for those who have not smoked in more than one year. Clients and providers may expect failure to quit as the rule, not the exception. Despite this misconception, this population can stop smoking at rates comparable to those in the general population. Nicotine use should be routinely and aggressively treated within behavioral health systems. To this end, DHCS and SFDPH BHS Pharmacy reimburse for and cover MNUD. Treatment should include both counseling and medication interventions as well as relapse support offered well past the point of cessation.

ASSESSMENT AND INTERVENTION PLANNING: A comprehensive approach to addressing quitting is summarized in Table 1. See Appendix 1 for resources available to clients and providers.

Table 1: “5 A’s” Algorithm

ASK	
Ask about nicotine use at every encounter	Identify all nicotine users and determine nicotine product used, quantity and current tobacco use status <u>Suggested Dialogue:</u> “Lisinopril is used to treat hypertension which is often made worse by nicotine products. Do you, or does someone in your household smoke or use nicotine?” “Anxiety is made worse by nicotine. Do you, or does someone in your household smoke or use nicotine?”
ADVISE	
In a clear, personalized, non-judgmental message advise every nicotine user to quit	<u>Suggested Dialogue:</u> “As your medical provider I want to encourage you to consider cutting down or quitting smoking/nicotine use.” “I’m concerned about your smoking/nicotine use and how that is affecting your goal to stop drinking alcohol. Did you know that some research has shown when you stop drinking and using nicotine products at the same time you can improve your chances of successfully quitting both?”
ASSESS	
Assess willingness to make a quit attempt in the next month Discuss client specific benefits Identify client’s position on readiness to change model	<u>Preparation:</u> Ready to make a quit attempt in the next 30 days → Proceed to Assist <u>Pre-Contemplative:</u> Not ready to quit in the next 6 months → Offer empathy and autonomy support. Offer to set a date in the future to check-in and provide motivational intervention.

	<p><u>Contemplative:</u> Ready to quit in the next 6 months → Schedule a follow up “what is getting in the way of you quitting now?”</p> <p><u>Maintenance:</u> Quit for longer than 6 months → Relapse prevention</p>
ASSIST	
Aid client in quitting	<p>See Appendix 2 Nicotine Cessation Client Interview</p> <ol style="list-style-type: none"> 1) Assess nicotine use history 2) Set a quit date “have you thought about a quit date?” <ol style="list-style-type: none"> a. Alternative: recommended practicing not smoking for 24 hours and seeing how it goes → then setting a quit date 3) Develop a quit plan which may include: <ol style="list-style-type: none"> a. Referral to resources (see Appendix 1) b. Identifying social support/resources c. Identifying pattern of use/triggers d. Planning coping skills and routine changes e. Exploring past attempts and identifying what worked well and what didn’t work well f. Determining preferred method of cessation (medication-assisted, cold turkey, reduction)
ARRANGE	
Schedule follow-up contact	<p>The highest risk of drop-out is within the first 7 days. Some evidence suggests more contact with mental health clients leads to more success.</p> <p>Actions during follow-up:</p> <ol style="list-style-type: none"> 1) Congratulate any successes 2) Review wins and challenges 3) Assess pharmacotherapy <p>Minimum follow-up frequency:</p> <ol style="list-style-type: none"> 1) First contact within the first week after the quit date 2) Second contact within the first month after quit date 3) Further contact as needed

NICOTINE WITHDRAWAL: Nicotine causes physical dependence and tolerance to the user. When quitting, nicotine withdrawal symptoms can peak in the first three days. Symptoms typically subside over the next three weeks but may continue for months. Symptoms include negative mood, urges to use, difficulty concentrating, increased appetite/weight gain, insomnia, irritability, anxiety, and restlessness. About half of nicotine users experience at least four of these symptoms when they quit. Any of the first-line pharmacologic agents described below are efficacious in reducing withdrawal symptoms. Clients that report prolonged cravings and withdrawal may be candidates for extended treatment or a combination of pharmacotherapy agents to target symptoms. See Appendix I for client resources regarding nicotine withdrawal and behavioral strategies to treat nicotine withdrawal symptoms and cravings.

NICOTINE USE DISORDER PHARMACOTHERAPY: The use of pharmacotherapy doubles the rate of abstinence from smoking compared to “cold-turkey” approaches. Three pharmacologic modalities are approved by the US Food and Drug Administration (FDA) for the treatment of tobacco-related NUD and include: nicotine replacement therapy (NRT), varenicline, and bupropion. These agents have different mechanisms of action and should be used with the consideration of client specific factors and preferences.

The goal of treatment is complete abstinence from smoking. Clients who fail to quit, but reduce the number of cigarettes per day, still incur the negative health risks associated with smoking. The health benefits of smoking reduction are not well studied, however clients that are able to reduce their smoking are more likely to quit in the future. Pharmacotherapy can even increase quit rates in light smokers (<5 cigarettes/day). Best outcomes are obtained when pharmacotherapy is used with behavioral counseling. See Appendix 3 for a summary of pharmacotherapy options available, common side effects, and dosing recommendations.

Recent RTCs and meta-analytic reviews suggest that e-cigarettes can help smokers quit at rates equivalent or higher than FDA approved MNUD. This option may be a viable harm reduction approach for some clients who can completely stop smoking with the use of e-cigarettes. Given the known short-term risks and the unknown long-term effects of e-cigarette use, no professional organizations currently endorse encouraging clients to adopt this approach to smoking cessation.

MNUD for e-cigarette use is an active area of research. RTCs and meta-analytic reviews indicate that varenicline may help people quit e-cigarettes while combination NRT or bupropion for this indication are inconclusive currently. Depending on the amount of nicotine consumed, some e-cigarette users may require higher than usual doses of NRT given some e-cigarettes can contain very high concentrations of nicotine and this is an active area of research. Please see this link for an example of an e-cigarette cessation MNUD guideline for adults:

<https://www.cdph.ca.gov/Programs/CCDCPHP/DCDIC/CTCB/CDPH%20Document%20Library/Community/CessationServicesandResources/VapingCessationGuideforPharmacists2019TRC.pdf>

NRT: NRT relieves nicotine withdrawal symptoms and is used to treat nicotine cravings. The combination NRT, using long-acting nicotine (transdermal patch) plus short-acting nicotine as needed (e.g. gum or lozenge) is more effective than either alone, however the choice is based largely on client preference. Additionally, NRT can safely be added to varenicline or bupropion to improve abstinence rates.

Side effects: Treatment side effects differ depending on route of administration. Thorough education of how to use each product is necessary to maximize benefit and limit side effects. For clients that experience vivid dreams with the nicotine transdermal patch, it is suggested to remove the patch at bedtime. Clients that complain of gastrointestinal symptoms with nicotine gum products should be educated on proper gum chewing technique to minimize oral ingestion of nicotine. Those with temporomandibular joint disease, poor dentition, or dental appliances may find nicotine lozenges easier to use compared to the gum.

Drug interactions: There are no clinically meaningful drug interactions with nicotine in any of the routes of administration described. Some clients may experience increased side effects (i.e. nausea, headache, indigestion) to NRT when used in combination with varenicline, however the mechanism to this interaction is unknown.

VARENICLINE: Varenicline is an oral, partial agonist of the nicotinic acetylcholine receptor reducing withdrawal symptoms including cravings and decreasing nicotine's reinforcing properties. Randomized controlled trials with varenicline suggest a more robust quit rate in the general population when compared to other monotherapy treatment modalities. When compared to combination NRT, varenicline did not show superior efficacy and produced similar quit rates. Varenicline allows for an alternative gradual approach to quitting for clients who are not able or willing to quit completely. The American Thoracic Society 2020 Guidelines for Initiating Pharmacologic Treatment in Tobacco-Dependent Adults strongly recommend varenicline over nicotine patches alone or bupropion alone for initiating treatment in adults with tobacco dependence. Those guidelines also strongly recommend starting varenicline for adults who are not ready to discontinue tobacco use rather than waiting until they are ready to stop tobacco use.

Side effects: Varenicline carried a boxed warning regarding potential neuropsychiatric side effects (e.g. behavioral changes, hostility, agitation, depressed mood, and suicidal thoughts and attempts) that was removed in 2016 after more subsequent studies demonstrated no difference in neuropsychiatric side effects compared with NRT or bupropion in people with NUD with or without psychiatric comorbidities.

Drug interactions: There are no clinically meaningful pharmacokinetic drug interactions with varenicline. Some clients may experience increased side effects (i.e. nausea, headache, indigestion) to NRT when used in combination with varenicline, however the mechanism to this interaction is unknown.

BUPROPION: Bupropion is an oral antidepressant medication that enhances norepinephrine and dopamine release in the brain. Its exact mechanism to aid in smoking cessation is not known. It can be considered for those with underlying depression but is also effective in those that are not diagnosed with depression. Bupropion can potentially reduce the amount of weight gain associated with smoking cessation and can be considered in clients for which this would be a concern. When used as monotherapy for the treatment of NUD, bupropion demonstrates slightly lower abstinence rates than other first-line therapies.

Side effects: Bupropion reduces the seizure threshold in a dose-dependent manner and should be avoided in clients with a known seizure disorder or predisposition to seizure (e.g. alcohol withdrawal, bulimia nervosa).

Drug Interactions: The major metabolic pathway for bupropion is via CYP2B6 and acts as a moderate inhibitor of CYP2D6. See Table 2 for more information about drug interactions.

Table 2: Bupropion Drug Interactions

Interaction	Clinical Concern
CYP2D6 substrates (ex: fluoxetine, tamoxifen, risperidone, beta-blockers, tramadol)	Increased concentrations of 2D6 substrates when co-administered with bupropion.
CYP2B6 inducers (ex: phenytoin, carbamazepine, rifampin)	Decrease in bupropion exposure when co-administered. Efficacy may be reduced.
MAO inhibitors in preceding 14 days or concurrent use of reversible MAO inhibitors	Increased risk of hypertensive reaction. Combination is contraindicated.

DURATION OF TREATMENT WITH NUD MAT: All clients who initiate pharmacotherapy should have initial follow-up via an office visit or phone call within one to two weeks to assess for positive responses, side effects, and medication optimization. The optimal duration of MNUD has not been established, even for longer-studied TUD interventions.

NRT manufacturers recommend treatment for two to three months, however BHS recommends continuing NRT until the client feels they are no longer at risk for relapse as continued pharmacotherapy can help prevent relapse. When treated with NRT for two months relapse rates are up to 80% during the first year following NRT cessation. It is estimated that approximately 50% of relapses could be averted with extended NRT use past the recommended guidelines. Long-term treatment with NRT (> 6 months) has not been associated with additional major health risks or adverse effects and is preferable in clients who are at high risk of relapsing to cigarette use. Clients with prolonged use may be at higher risk of nicotine withdrawal when stopping their NRT and should be tapered using a lower dose patch, gum, or lozenge. Insurance companies may not cover smoking cessation medications beyond three months and may require additional authorizations for continued use.

Clients may benefit from continuing varenicline after the recommended 12 weeks to prevent relapse. Safety and efficacy have been established up to 6 months of continued use.

The duration of treatment with bupropion may be influenced by other indications outside of NUD (i.e. depression, ADHD) that would require longer term treatment. The recommended duration of treatment with bupropion for TUD is 7-12 weeks, however safety and efficacy has been established up to 12 months of continued use.

SELECTION OF MNUD: Appendix 4 provides decision guidance in selecting pharmacologic therapy. Recommendations are based on RCTs, availability, and other practical considerations. Client preference and co-morbid conditions should be considered when choosing an initial agent as the three different treatment modalities have relatively comparable abstinence rates ranging from 20-35%. Clients with no response to the initial agent at four weeks should have a re-assessment of their treatment to determine if a change in medication is indicated. Medication dosing and administration should be reviewed to ensure adherence and proper use. Those with a partial response to the initial treatment may benefit from the addition of a second agent based residual symptoms such as ongoing withdrawal or cravings. For clients who successfully quit then relapse, the medication that previously worked should be considered again.

OFF-LABEL AGENTS WITH INSUFFICIENT EVIDENCE TO RECOMMEND AS FIRST-LINE THERAPY

Nortriptyline: Nortriptyline is a tricyclic antidepressant medication with modest evidence for use in TUD. It can be considered for clients who require adjunctive treatment to a first-line therapy. It may be poorly tolerated in many clients due to sedation, dry mouth, constipation, and dizziness. Nortriptyline should be avoided in clients at risk of arrhythmias, bipolar disorder, and those at risk of overdose.

Clonidine: Clonidine has limited evidence to support its use in smoking cessation with conflicting efficacy study results. Side effects such as drowsiness, fatigue, and dry mouth may further limit its use. A drawback to clonidine is its risk of withdrawal symptoms, including rebound hypertension, diaphoresis, insomnia, headache and anxiety/agitation. Immediate release oral clonidine products should be slowly dose reduced over 6-10 days. Use of clonidine oral tablets should be considered carefully with regards to clients' ability to tolerate a BID or TID regimen and ability to taper off once treatment is complete

CO-OCCURRING DISORDERS AND SPECIAL POPULATIONS

Cardiovascular disease: In those with stable cardiovascular disease (CVD) the same treatments can safely be used as the general population. Caution should be used with NRT in the first two weeks immediately following a myocardial infarction because of its potential to increase cardiac demand.

Pregnancy: Smoking during pregnancy is the most important modifiable risk factor associated with adverse pregnancy outcomes. Smoking cessation before pregnancy is most beneficial or early in pregnancy is more beneficial for the mother and fetus, however quitting at any time in pregnancy can provide benefit. The U.S. Clinical Practice Guideline and American College of Obstetrics and Gynecology state that pregnant smokers or nicotine users should be encouraged to quit without medication based on insufficient evidence of effectiveness and theoretical concerns with safety. It is reasonable to consider pharmacotherapy in women who are unable to quit and are at high risk for continued smoking throughout pregnancy. In pregnancy, NRT should be used with the clear goal of the client to quit smoking and with close supervision after discussing the risks of continued smoking against possible risks of NRT. There is no strong evidence that pregnant smokers who use NRT are at higher risk of adverse events than pregnant smokers not using NRT. Bupropion can also be considered in this population after discussing the risks and benefits of treatment. Bupropion is known to cross the placenta and is associated with a low risk of teratogenicity. Varenicline is not recommended for use in pregnancy due to limited safety information.

Lactation: The Committee on Drugs of the American Academy of Pediatrics recommends NRT as the preferred pharmacotherapy in breastfeeding women. Although nicotine passes into breast milk, the risks associated with smoking are deemed to be of greater harm. Nicotine may have adverse effects on the infant, such as interfering with lung development and increasing the risk of sudden infant death syndrome. Bupropion and its active metabolites are present at low concentrations in breast milk. It may be used in breastfeeding women after discussion of the potential risks of exposure that include vomiting, jitteriness, sedation, and potential seizures. Data on varenicline in humans is not available and thus should be avoided in breastfeeding women.

Co-occurring mental illness: Those with mental illness are often more nicotine dependent than the general population and may need higher doses, longer duration of treatment, and combined medications to optimize therapy. Clients on medications for the treatment of their mental illness may incur changes in medication blood levels depending on their smoking status. This drug interaction is due to the induction of CYP 1A2 secondary to the hydrocarbons found in smoke that are inhaled from cigarettes; therefore, nicotine replacement therapy would not have the same effect. See Appendix 5 for a summary of psychotropic medications susceptible to this interaction. Monitoring medication side effects and symptoms of illness are necessary as a client quits smoking or relapses to determine if a dose change is required.

Depression: Consider using bupropion for clients with a diagnosis of depression although bupropion's efficacy has been shown independent of depressive symptoms. The largest smoking cessation study in adults did not demonstrate differences in neuropsychiatric adverse events in those with or without depression between those treated with varenicline or bupropion or NRT plus placebo and varenicline demonstrated higher efficacy compared to bupropion or NRT.

Schizophrenia: For individuals with NUD and comorbid schizophrenia, varenicline or bupropion, with or without NRT, are recommended first line agents. Bupropion should be used with caution and close monitoring in these situations since it can worsen positive psychotic symptoms.

Bipolar disorder: For individuals with bipolar disorders and NUD, NRT, bupropion, and varenicline are effective and well tolerated pharmacotherapies when paired with behavioral support. Caution with the use of bupropion in this population may be warranted given the theoretical potential of switching to manic/hypomanic episodes although this has not been found in larger studies.

Anxiety disorders: Varenicline showed higher efficacy with greater abstinence rates compared to bupropion or NRT, although each was also effective, and did not increase anxiety.

Substance use disorders: Clients with a co-occurring substance use disorder have the highest prevalence of smoking among people with mental illness reaching as high as 98%. Some evidence supports treating NUD improves treatment of other substance use disorders. Clients with comorbid substance use disorders have a lower abstinence rate than the general population and may benefit from more intensive behavioral interventions. Active substance abuse precludes clients from enrollment into most prospective studies, therefore other patient factors, like comorbidities, should be considered in treatment selection.

Adolescents: Initially, the focus in this group had been primary prevention strategies through public health education and regulatory legislative actions. However, psychosocial and pharmacological interventions are also used to treat NUD in adolescents. The American Academy of Pediatrics (AAP) recommends NRT for NUD in youth despite a lack of FDA approvals citing the effectiveness of NRT in adults and the severe negative health consequences of tobacco and e-cigarette use as the rationale for advocating NRT for minors. In limited studies, the effectiveness of NRT in youth is more modest than in adults and there is no evidence of serious harm from NRT in adolescents. As with adults, the only absolute contraindication for NRT in youth is hypersensitivity. Other relative contraindications like

cardiovascular disease, diabetes, and hyperthyroidism should be considered in minors as well but in general the risks of continued tobacco or e-cigarette use far outweigh the potential risks of NRT. Lower doses of nicotine patches and gum should be used in those with body weight less than 45 kilograms. Youth require a prescription from a healthcare provider to access all forms of NRT since OTC NRT is only available to those 18 years and older. Varenicline and bupropion should be used at the discretion of the clinician in collaboration with the minor and guardian(s) as evidence in this age group is limited. Prescribed MNUD for minors is covered by Medi-Cal. Minors 12-17 years old can consent to MNUD treatment and parental consent is also encouraged. Given known short-term and unknown long-term risks of e-cigarette use, their use in harm reduction approaches to minor tobacco smokers is not advisable. Furthermore, e-cigarettes are not legal to purchase for those under 21 years old and there are no prescribable e-cigarettes, their use in this population is not possible. The AAP strongly advises against the use of e-cigarettes in smoking cessation for minors.

Although adolescents' use of e-cigarettes is very likely less harmful than combustible tobacco, clear evidence exists that this use is associated with medical and mental health symptoms including anxiety, depression, and suicidal ideation and behavior. No current consensus on MNUD for e-cigarette-using youth is available but the AAP position advocates NRT for this population since it is less risky than continued e-cigarette use. Depending on the amount of nicotine consumed, some e-cigarette users may require higher than usual doses of NRT given some e-cigarettes can contain very high concentrations of nicotine and this is an active area of research. Varenicline also helped adolescents quit using e-cigarettes in a recent RCT. Please see this link for an example of an e-cigarette cessation guideline for adults that may assist in treating e-cigarette use in adolescents:

<https://www.cdph.ca.gov/Programs/CCDPHP/DCDIC/CTCB/CDPH%20Document%20Library/Community/CessationServicesandResources/VapingCessationGuideforPharmacists2019TRC.pdf>

Older adults: There are no meaningful differences in safety or efficacy in older adults.

Hepatic impairment: NRT can safely be used in hepatic impairment although clearance may be reduced. Bupropion should be used with caution in clients with hepatic impairment and dose reductions are recommended for those with moderate-severe impairment. No dosage adjustment is necessary for varenicline.

Renal impairment: No dosage adjustment is necessary for NRT. Bupropion side effects should be monitored in those with reduced renal clearance. Varenicline requires dose reduction for clients with creatinine clearance less than 30 ml/min. See Appendix 3 for recommendations.

REFERENCES AND FURTHER READING

Alvarez Gutierrez FJ, Ferrer Galvan M, Ruiz Bernal AP, et al. Predictors of 10-year smoking abstinence in smokers abstinent for 1 year after treatment. *Addiction*. 2016;111:545-551.

American Academy of Pediatrics. Nicotine Replacement Therapy and Adolescent Patients: Information for Pediatricians. Updated May 2024. https://www.aap.org/en/patient-care/tobacco-control-and-prevention/youth-tobacco-cessation/nicotine-replacement-therapy-and-adolescent-patients/?srsltid=AfmBOoroLxkSlee_-N069utfE1F862vDiwg19XFtPJy6X0-MvOGNLRsz

Bandiera FC, Anteneh B, Le T, et al. Tobacco-related mortality among persons with mental health and substance abuse problems. *PloS One*. 2015;10 e0120581.

Butler AR, Lindson N, Livingstone-Banks J, Notley C, Turner T, Rigotti NA, Fanshawe TR, Dawkins L, Begh R, Wu AD, Brose L, Conde M, Simonavičius E, Hartmann-Boyce J. Interventions for quitting vaping. *Cochrane Database of Systematic Reviews* 2025, Issue 1. Art. No.: CD016058. DOI: 10.1002/14651858.CD016058.pub2. Accessed 22 May 2025.

Cahill K, Stevens S, Perera R, Lancaster T. Pharmacological interventions for smoking cessation: an overview and network meta-analysis. *Cochrane Database Syst Rev*. 2013;5:CD009329.

Evins AE, Cather C, Reeder HT, Evohr B, Potter K, Pachas GN, Gray KM, Levy S, Rigotti NA, Iroegbulem V, Dufour J, Casottana K, Costello MA, Gilman JM, Schuster RM. Varenicline for Youth Nicotine Vaping Cessation: A Randomized Clinical Trial. *JAMA*. 2025 Apr 23:e253810. doi: 10.1001/jama.2025.3810. Epub ahead of print. PMID: 40266580; PMCID: PMC12019676.

Fiore MC, Jaén CR, Baker TB, et al. (2008). Treating tobacco use and dependence: 2008 update. US Department of Health and Human Services, Rockville, MD. Public Health Service. https://www.ahrq.gov/sites/default/files/wysiwyg/professionals/clinicians-providers/guidelines-recommendations/tobacco/clinicians/update/treating_tobacco_use08.pdf

Fornaro, M., et al. The prevalence, odds, predictors, and management of tobacco use disorder or nicotine dependence among people with severe mental illness: Systematic review and meta-analysis. 2022. *Neuroscience and biobehavioral reviews*, 132, 289–303.

Grant BF, Hasin DS, Chou P, et al. Nicotine dependence and psychiatric disorders in the United States; results from the national epidemiologic survey on alcohol and related conditions. *Arch Gen Psychiatry*. 2004;61:1107-1115.

Hajek P, West R, Foulds J, et al. Randomized comparative trial of nicotine polacrilex, a transdermal patch, nasal spray, and an inhaler. *Arch Intern Med*. 1999;159:2033–2038.

Han B, Compton, M, Blanco C. Tobacco use and 12-month suicidality among adults in the United States. *Nicotine Tob Res*. 2017;19:39-48.

Harrison-Woolrych M, Paterson H, Tan M. Exposure to the smoking cessation medicine varenicline during pregnancy: a prospective nationwide cohort study. *Pharmacoepidemiol Drug Saf* 2013;22:1086–92

Kleber HD, et al. (2006). Treatment of patients with substance use disorders, second edition. American Psychiatric Association.

Knudsen HK, Studts JL, Boyd S, et al. Structural and cultural barriers to the adoption of smoking cessation services in addiction treatment organizations. *J of Addict Dis.* 2010;29:294-305.

Kroon LA. Drug interactions with smoking. *Am J Health-Syst Pharm.* 2007;64:1917-21.

Kypriotakis G, Cinciripini PM, Green CE, Lawrence D, Anthenelli RM, Minnix JA, Beneventi D, Morris C, Karam-Hage M, Blalock JA. Effects of Varenicline, Bupropion, Nicotine Patch, and Placebo on Treating Smoking Among Persons With Current or Past Major Depressive Disorder: Secondary Analysis of a Double-Blind, Randomized, Placebo-Controlled Trial. *Am J Psychiatry.* 2025 Feb 1;182(2):174-186. doi: 10.1176/appi.ajp.20230855. Epub 2024 Dec 11. PMID: 39659160.

Leone FT et al. Initiating Pharmacologic Treatment in Tobacco-Dependent Adults. An Official American Thoracic Society Clinical Practice Guideline. *American journal of respiratory and critical care medicine.* 2020. 202(2), e5–e31.

Lindson N, Butler AR, McRobbie H, Bullen C, Hajek P, Wu AD, Begh R, Theodoulou A, Notley C, Rigotti NA, Turner T, Livingstone-Banks J, Morris T, Hartmann-Boyce J. Electronic cigarettes for smoking cessation. *Cochrane Database of Systematic Reviews* 2025, Issue 1. Art. No.: CD010216. DOI: 10.1002/14651858.CD010216.pub9.

Livingston JA, Chen CH, Kwon M, Park E. Physical and mental health outcomes associated with adolescent E-cigarette use. *J Pediatr Nurs.* 2022 Feb 1;64:1-17.

McKelvey K, Thrul J, Ramo D. Impact of quitting smoking and smoking cessation treatment on substance use outcomes; An updated and narrative review. *Addict Behav.* 2017;65:161-170.

Murkett R, Rugh M and Ding B. Nicotine products relative risk assessment: an updated systematic review and meta-analysis [version 2; peer review: 1 approved, 1 approved with reservations]. *F1000Research* 2022, 9:1225 (<https://doi.org/10.12688/f1000research.26762.2>)

National Institute for Clinical Excellence (NICE). (2013). Smoking: acute, maternity and mental health services. NICE Public Health Guidance 48. Available online at: <https://www.nice.org.uk/guidance/ph48/resources/smoking-acute-maternity-and-mental-health-services-pdf-1996364658373>

Palmer AM, Tomko RL, Squeglia LM, Gray KM, Carpenter MJ, Smith TT, Dahne J, Toll BA, McClure EA. A pilot feasibility study of a behavioral intervention for nicotine vaping cessation among young adults delivered via telehealth. *Drug Alcohol Depend.* 2022 Mar 1;232:109311.

Richardson JL, Stephens S, Yates LM, Diav-Citrin O, Arnon J, Beghin D, et al. Pregnancy outcomes after maternal varenicline use; analysis of surveillance data collected by the European Network of Teratology Information Services. *Reprod Toxicol* 2017;67:26–34

Stead LF, Koilpillai P, Fanshawe TR, et al. Combined pharmacotherapy and behavioral interventions for smoking cessation. *Cochrane Database Syst Rev.* 2016;24:3:CD008286.

Szerman N, Parro C, Vega P, Basurte-Villamor I, Ruiz-Veguilla M. Tobacco use disorder in patients with other mental disorders: a dual disorder perspective from clinical neuroscience. *Front Psychiatry.* 2024 Oct 11;15:1427561. doi: 10.3389/fpsyt.2024.1427561. PMID: 39465048; PMCID: PMC11502350.

Tuisku A, Rahkola M, Nieminen P, Toljamo T. Electronic Cigarettes vs Varenicline for Smoking Cessation in Adults: A Randomized Clinical Trial. JAMA Intern Med. 2024 Aug 1;184(8):915-921. doi: 10.1001/jamainternmed.2024.1822. Erratum in: JAMA Intern Med. 2024 Aug 1;184(8):993. doi: 10.1001/jamainternmed.2024.3981. PMID: 38884987; PMCID: PMC11184496.

Tulloch HE, Pipe AL, Clyde MJ, et al. The quit experience and concerns of smokers with psychiatric illness. AM J of Prev Med. 2016;50:709-718.

University of California San Francisco School of Pharmacy. (2018). The Rx for change: clinician-assisted tobacco cessation curriculum. <http://rxforchange.ucsf.edu>

U.S. Department of Health and Human Services. (2014). Reducing the health consequences of smoking: 50 years of progress: a report of the surgeon general. US Department of Health and Human Services, Rockville, MD. Available online at: <https://www.surgeongeneral.gov/library/reports/50-years-of-progress/full-report.pdf>

U.S. Preventive Services Task Force. Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Persons: US Preventive Services Task Force Recommendation Statement. JAMA. 2021;325(3):265–279.

Vahratian A, Briones EM, Jamal A, Marynak KL. Electronic cigarette use among adults in the United States, 2019–2023. NCHS Data Brief, no 524. Hyattsville, MD: National Center for Health Statistics. 2025. DOI: <https://dx.doi.org/10.15620/cdc/174583>

Weinberger AH, Platt J, Esan H, et al. Cigarette smoking is associated with increased risk of substance use disorder relapse. A nationally representative, prospective longitudinal investigation. J Clin Psych. 2017; 78:e152-e160.

Wennike, P, et al. Smoking reduction promotes smoking cessation: results from a double blind, randomized, placebo-controlled trial of nicotine gum with 2-year follow-up. Addiction. 2003;98:1395–402.

Wu Q, Gilbody S, Peckham E, et al. Varenicline for smoking cessation and reduction in people with severe mental illness: systematic review and meta-analysis. Addiction. 2016 Sep;111:1554-67.

Ziedonis D, Hitsman B, Beckham JC, et al. Tobacco use and cessation in psychiatric disorders: national institute of mental health report. Nicotine Tob Res. 2008;10:1691–1715.

APPENDIX 1: LOCAL RESOURCES

Program Name	Overview
Free Smoking Cessation Groups	
San Francisco Tobacco Free –Project (TFP) https://www.sf.gov/san-francisco-tobacco-free-project 25 Van Ness, Avenue, 5 th floor San Francisco, CA 94102 Phone: (628) 206-7668 Email: tfp-chep@sfdph.org	This program provides free cessation support through quit-smoking classes, coaching, and “SF Quit! Kits” with helpful tools and resources. TFP also leads public health advocacy, including successful efforts to ban flavored tobacco and limit retail sales near schools.
We Breathe https://californialgbtqhealth.org/about-us/we-breathe/ 1127 11 th Street, Suite 925 Sacramento, CA 95814 Email: info@californialgbtqhealth.local Phone: 916-497-0923	We Breathe provides expertise on working with LGBTQ communities, preventing and reducing tobacco use among LGBTQ Californians, and addressing tobacco-related health disparities within LGBTQ communities by fostering culturally competent strategies and policies.
Northern California Intergroup of Nicotine Anonymous https://www.nica-norcal.org/ 2261 Market Street, #229-A San Francisco, CA 94114	A 12-step help program.
Free Phone and Online Programs	
Kick It California (KIC) https://kickitca.org/ English: 1-800-300-8086 Spanish: 1-800-600-8191 Mandarin & Cantonese: 1-800-838-8917 Vietnamese: 1-800-778-8440 Korean: 1-800-556-5564 Deaf/Hearing Impaired: 1-800-933-4TDD Text Program: “quit smoking” to 66819 “quit vaping” to 668919	KIC offers free quit support via multiple channels such as phone, text messaging, mobile apps, and online chat plus self-help materials. Online help is available in six languages to help clients quit smoking.
quitSTART smartphone app https://www.cdc.gov/tobacco/campaign/tips/quit-smoking/quitstart-app/	A free smartphone app is a product of Smokefree.gov, a smoking cessation resource created by the Tobacco Control Research Branch at the National Cancer Institute in collaboration with the FDA. The app takes personal information about a person’s smoking history and gives tips, inspiration, and challenges to assist in becoming smokefree.
Smokefree.gov https://smokefree.gov/ Text Program: “quit” to 47848	An online website created by the Tobacco Control Research Branch at the National Cancer Institute that provides free, accurate, evidence-based information and professional assistance to help support the immediate and long-term needs of people trying to quit smoking. Smokefree.gov offers free text messaging 6-8 weeks program that give 24/7 encouragement, advice, and tips for becoming smokefree. It also provides specialized resources for women, veterans, and teens.
Resources for Providers	

<p>Rx for Change http://rxforchange.ucsf.edu/</p>	<p>Clinician-Assisted Tobacco Cessation is a comprehensive tobacco cessation training program that equips health professional students and practicing clinicians, of all disciplines, with evidence-based knowledge and skills for assisting clients with quitting.</p> <p>UCSF and the Purdue University College of Pharmacy openly shares the Rx for Change materials with others at no cost; however, all persons who receive any component of the Rx for Change program must complete an online registration process. Rx for Change can be used only for non-commercial teaching and research purposes and cannot be used for profit.</p>
<p>Smoking Cessation Leadership Center https://smokingcessationleadership.ucsf.edu/</p>	<p>A national program office of the Robert Wood Johnson Foundation at the University of California, San Francisco reduces disparities in tobacco use and increases cessation through community partnership. Their goal is to drive health systems change by eliminating barriers to access to tobacco treatment, promoting tobacco policy that supports cessation, and providing education and training.</p>
<p>Kick It California (KIC) 1800-300-8086 https://kickitca.org/education-training</p> <p>e-Referral link: https://kickitca.org/patient-referral</p>	<p>Kick It California (KIC) provides training for the California Smokers' Helpline. KIC helps organizations with professional training, structure and provides the following free services:</p> <ul style="list-style-type: none"> • Providers can refer tobacco users to KIC to get a free, personal quit plan from trained coaches via the e-referral link. • Free training and technical assistance such as webinars, continuing education opportunities, and training for integrating cessation services into practice. • Provider Toolkits complete with webinars and client educational materials (digital and print materials).

APPENDIX 2:

NICOTINE CESSATION CLIENT INTERVIEW FORM

Date: Time: Provider's name:

Section 1: Patient information

Name (Last, First): Date of birth: Gender:

Primary phone number: Home address:

Insurance provider:

BIN	PCN	Cardholder ID	Group number

PCP name: PCP phone number:

Section 2: Medical conditions

Current medical conditions:

- 1
- 2
- 3
- 4
- 5

Past medical conditions:

- 1
- 2
- 3
- 4
- 5

Section 3: High-risk screening

- | | | | |
|---|---|----|-----|
| 1 | Pregnant or planning to become pregnant in the next 6 months? | No | Yes |
| 2 | Heart attack in past 2 weeks? | No | Yes |
| 3 | History of arrhythmias or irregular heartbeat? | No | Yes |
| 4 | Unstable angina or chest pain with strenuous activity? | No | Yes |

IF YES to any,
consult with or
refer patient to
PCP.

Section 4: Other history

- 1 Family history of nicotine use or nicotine-related diseases?
- 2 Other medical conditions? (e.g. Do you have serious dental problems or have you been diagnosed with TMJ [pain or popping of the jaw]? If yes, avoid gum. Do you have a history of severe acid reflux or stomach upset? If yes, monitor for exacerbation from gum or lozenges.)

Section 5: Medications and allergies/hypersensitivities

Current medications:

Allergies/Hypersensitivities:

Section 6: Assess Tobacco Use History

ASK: What types of nicotine do you use?

Type	How much and how often (e.g. # cigarettes, # mg nicotine per day)?	How long used?
Cigarettes		
E-cigarettes/JUUL/vaping		
Smokeless tobacco (dip, chew)		
Cigars or cigarillos		
Other:		

ASK: How many minutes after you wake up do you have your first cigarette/tobacco/nicotine?

ASK: Any recent changes in your tobacco/nicotine use?

ASK: Have you tried to quit before? **Y N**

- **If YES:** How many times? When was last quit attempt? Longest quit attempt?

ASK: Did you call the tobacco quit line or participate in any other form of counseling? **Y N**

- **If YES:** What did you like, or not like, about it?

ASK: What quitting medicines have you tried in the past? Discuss effectiveness, withdrawal symptoms, how med was taken (daily and duration), overall experience (does it make sense to try it again?).

ASK: Main reasons for returning smoking/tobacco/nicotine use? Anticipated challenges this/next time?

- What would you say are the good things about nicotine? What do you like about nicotine?
- What are the not so good things about nicotine? What are your main reasons to quit?

ASK: Are you ready to set a quit date? **Y N** (if yes, record quit date below under “Documentation”)

- On a scale from 0 – 10, (where “0” is not ready to quit smoking and “10” is ready to quit smoking), what score would you give yourself right now?
- If not 0, you gave yourself a score of _____. Why do you think _____ and not a lower number?
- If 0, is there anything that would help raise your score to a 1 or 2?

DOCUMENTATION

IF READY TO SET QUIT DATE, complete the following and initial to the left of each requirement.

- ____ Discuss medication options and select treatment
- ____ Ask patient to choose a quit date (if using bupropion SR or varenicline, consider medication start date)

Patient’s planned quit date is:

- ____ Refer patient to Tobacco Quitline (1-800-QUIT NOW) or other program:
- ____ Document treatment plan
- ____ Schedule follow-up appointment within 2 weeks of quit date:

Date and time:

Circle one: In-person or Telephone **ASK:** Confirm preferred contact #

- ____ Advise patient to follow-up with PCP
- ____ Contact patient’s PCP within 3 business days

APPENDIX 3: FDA-APPROVED MEDICATIONS FOR TOBACCO USE DISORDER

Product	Dosage^	Common Side Effects	Availability	Counseling Points	Advantages	Disadvantages
Short-Acting Products						
Nicotine Gum 2 mg, 4 mg	For the following weeks, use gum as needed for cravings or urges to smoke: Wks 1-6 every 1-2 hrs Wks 7-9 every 2-4 hrs Wks 10-21 every 4-8 hrs <i>If 1st cig within 30 min of waking: use 4mg</i> <i>If 1st cig after 30 min of waking: use 2mg</i> Use at least 9/day for first 6 weeks if using as monotherapy NTE: 24 pcs/day *for combination NRT, start with 2 mg dose	Mouth/jaw soreness, indigestion, hiccups Dizziness/ lightheadedness N/V, with incorrect technique	Prescription and OTC	<ul style="list-style-type: none"> Chew each piece slowly Park between cheek and gum when peppery or tingling sensation appears (~15–30 chews) Resume chewing when tingle fades Repeat chew/park steps until most of the nicotine is gone (tingle does not return, generally 30 min) Park in different areas of mouth <p>No food or beverages 15 minutes before or during use</p>	<ul style="list-style-type: none"> Might serve as an oral substitute for tobacco Can be titrated to manage withdrawal symptoms Can be used in combination with other agents to manage situational urges Relatively inexpensive 	<ul style="list-style-type: none"> Frequent dosing can be problematic with significant dental work Proper chewing technique is required for effectiveness <p>PRECAUTIONS</p> <ul style="list-style-type: none"> Avoid use with TMJ Recent (\leq 2 weeks) myocardial infarction Serious underlying arrhythmias Serious worsening angina pectoris

^NRT dosing is based on recommendations from package inserts. Clients can safely smoke and continue to use NRT beyond package instructions. We recommend using NRT until the client feels ready to step down therapy or stop treatment with minimal risk for relapse.

Product	Dosage [^]	Common Side Effects	Availability	Counseling Points	Advantages	Disadvantages
Nicotine Lozenge 2 mg, 4 mg	For the following weeks, take one lozenge* as needed for cravings or urges to smoke: Wks 1-6 every 1-2 hrs Wks 7-9 every 2-4 hrs Wks 10-21 every 4-8 hrs NTE: 20 pcs/day <i>If 1st cig within 30 mins of waking: use 4 mg</i> <i>If 1st cig after 30 mins of waking: use 2 mg</i> *for combination NRT, start with 2 mg dose Use at least 9/day for first 6 weeks if using as monotherapy	Mouth and throat soreness, indigestion, hiccups	Prescription and OTC	<ul style="list-style-type: none"> Allow to dissolve slowly (20–30 minutes for standard; 10 minutes for mini lozenge) Nicotine release may cause a warm, tingling sensation Do not chew or swallow Occasionally rotate to different areas of the mouth No food or beverages 15 minutes before or during use 	<ul style="list-style-type: none"> Might serve as an oral substitute for tobacco Can be titrated to manage withdrawal symptoms Can be used in combination with other agents to manage situational urges Relatively inexpensive 	<ul style="list-style-type: none"> Frequent dosing Gastrointestinal side effects can compromise use of lozenge <p>PRECAUTIONS</p> <ul style="list-style-type: none"> Recent (\leq 2 weeks) myocardial infarction Serious underlying arrhythmias Serious worsening angina pectoris Avoid in soy allergy
Short Acting Products						
Nicotine Nasal Spray 10 mg/ml metered spray	Spray 1-2 sprays in each nostril every hour as needed for nicotine cravings. <i>One dose= 1 spray in each nostril, each spray delivers 0.5 mg.</i> NTE: 5 doses/hr or 40 doses/day Use at least 8 doses for 6-8 weeks (for monotherapy)	Nasal irritation, change in sense of smell/taste, cough, tearing, headache	Prescription Only	<ul style="list-style-type: none"> Avoid with underlying chronic nasal disorders (rhinitis, nasal polyps, sinusitis) or severe reactive airway disease Do not sniff or inhale the spray when administering 	<ul style="list-style-type: none"> Can be titrated to rapidly manage withdrawal Can be used in combination with other agents to manage situational urges Shown to be more efficacious than other short-acting NRT 	<ul style="list-style-type: none"> Frequent dosing Nasal irritation can be problematic Relatively expensive <p>PRECAUTIONS</p> <ul style="list-style-type: none"> Avoid with underlying chronic nasal disorders Recent (\leq 2 weeks)

[^]NRT dosing is based on recommendations from package inserts. Clients can safely smoke and continue to use NRT beyond package instructions. We recommend using NRT until the client feels ready to step down therapy or stop treatment with minimal risk for relapse.

Product	Dosage [^]	Common Side Effects	Availability	Counseling Points	Advantages	Disadvantages
						myocardial infarction <ul style="list-style-type: none"> • Serious underlying arrhythmias Serious of worsening angina pectoris
Long-Acting Products						
Nicotine Transdermal Patch 7 mg, 14 mg, 21 mg (24-hr release) patches	Place one patch on dry skin every 24 hours as directed*: 21 mg/24 hrs x 4 wks, 14 mg/24 hrs x 2 wks, 7 mg/24 hrs x 2 wks Start with 21 mg patch if smoking > 10 cigs/day and 14 mg patch is ≤ 10 cigs NTE: 21 mg/day (Higher doses may be considered on an individual basis for those that smoke >20 cigs or continue to smoke while using the patch)	Local skin reaction, insomnia, vivid dreams	Prescription and OTC	<ul style="list-style-type: none"> • Rotate patch application site daily; do not apply a new patch to the same skin site for at least one week • May wear patch for 16 hours if client experiences sleep disturbances (remove at bedtime) • Not recommended for use by clients with dermatologic conditions (i.e. psoriasis, eczema, atopic dermatitis) 	<ul style="list-style-type: none"> • Once-daily dosing • Discreet appearance • Can be used in combination with other agents • Delivers consistent nicotine levels over 24 hours • Relatively inexpensive 	<ul style="list-style-type: none"> • When used as monotherapy, cannot be titrated to acutely manage withdrawal symptoms PRECAUTIONS <ul style="list-style-type: none"> • Avoid with chronic dermatologic conditions (psoriasis, Eczema, atopic dermatitis) • Recent (<= 2 weeks) myocardial infarction • Serious underlying arrhythmias Serious of

[^]NRT dosing is based on recommendations from package inserts. Clients can safely smoke and continue to use NRT beyond package instructions. We recommend using NRT until the client feels ready to step down therapy or stop treatment with minimal risk for relapse.

Product	Dosage [^]	Common Side Effects	Availability	Counseling Points	Advantages	Disadvantages
						worsening angina pectoris
Oral Medications						
Bupropion Sustained Release (SR) 150 mg tablet	Begin therapy 1–2 weeks prior to quit date: Take 150 mg PO qAM x 3 days, then 150 mg PO BID Contraindications: <ul style="list-style-type: none"> Seizure disorder Current or prior diagnosis of bulimia or anorexia nervosa Simultaneous abrupt discontinuation of alcohol or sedatives/benzodiazepines MAO inhibitors in preceding 14 days; concurrent use of reversible MAO inhibitors 	Insomnia, dry mouth, nervousness/difficulty concentrating, nausea, dizziness, constipation, seizures	Prescription Only	<ul style="list-style-type: none"> Allow at least 8 hours between doses Avoid bedtime dosing to minimize insomnia Use with caution in clients with concomitant therapy with medications/conditions known to lower the seizure threshold 	<ul style="list-style-type: none"> May reduce weight gain associated with quitting May be beneficial in clients with co-morbid depression Once daily bupropion extended-release (XL) may be used in place of the SR formulation to enhance adherence Can be used in combination with NRT Dose tapering is not necessary 	<ul style="list-style-type: none"> Seizure risk is increased Several contraindication and precautions preclude use in some clients (see below) No emergent relief
Varenicline 0.5 mg, 1 mg tablets	Start 1 week before quit date: On days 1-3, take 0.5 mg PO qAM On days 4-7, take 0.5 mg PO BID On weeks 2-12, take 1 mg PO BID Dosing adjustment is necessary for clients with severe renal impairment (< 30 ml/min) to a maximum of 0.5 mg BID	Nausea, vomiting, sleep disturbances (insomnia, abnormal/vivid dreams), constipation, flatulence, taste alteration	Prescription Only	<ul style="list-style-type: none"> Take dose after eating and with a full glass of water Clients that incur sleep disturbances can be instructed to take the evening dose earlier in the day or may require skipping the evening dose Avoid alcohol while taking Gradual approach with no defined quit date or if clients continue to smoke 	<ul style="list-style-type: none"> Offers a different mechanism of action for clients who failed other agents Dose tapering is not necessary May provide greater efficacy in the general population compared to other monotherapy Can be used in combination with NRT 	<ul style="list-style-type: none"> Cost of treatment No emergent relief Clients should be monitored for potential neuropsychiatric symptoms

[^]NRT dosing is based on recommendations from package inserts. Clients can safely smoke and continue to use NRT beyond package instructions. We recommend using NRT until the client feels ready to step down therapy or stop treatment with minimal risk for relapse.

Product	Dosage^	Common Side Effects	Availability	Counseling Points	Advantages	Disadvantages
				past quit date: Titrate dose as above to 1 mg PO BID. Clients should reduce smoking by 50% in first 4 weeks, then additional 50% in following 4 weeks, continued until abstinence in 12-24 weeks	agents	
Off-Label Agents						
Nortriptyline 10 mg, 25 mg, 50 mg, 75 mg capsules	Take 25 mg PO at bedtime. Increase dose as tolerated by 25 mg/week up to 75-125 mg Contraindications MAO inhibitors in preceding 14 days; concurrent use of reversible MAO inhibitors	Dry mouth, orthostatic hypotension, cardiac arrhythmia, constipation, urinary retention, sexual dysfunction, sedation	Prescription Only	<ul style="list-style-type: none"> • Begin therapy 4 weeks prior to quit date • Take at bedtime to avoid daytime sedation • Should be used with caution in clients with a history of cardiovascular disease • Should be tapered off 	<ul style="list-style-type: none"> • May be beneficial in clients with co-morbid depression, anxiety, insomnia, or chronic pain • Relatively inexpensive • Can be used in combination with NRT 	<ul style="list-style-type: none"> • High side effect burden • Dangerous in overdose • May require blood level monitoring
Clonidine 0.1 mg, 0.2 mg, 0.3 mg tablets 0.1 mg/24hr, 0.2 mg/24 hr, 0.3 mg/24 hr patches	Oral: Can be started at 0.1 mg PO BID and titrated to 0.4 mg divided TID Patch: Apply 0.1 mg/24 hr patch to dry skin every 7 days. Can be titrate based on effect and tolerability.	Decreased heart rate, sedation, orthostatic hypotension, dizziness, dry mouth, constipation	Prescription Only	<ul style="list-style-type: none"> • Begin therapy 48-72 hours before quit attempt • Do not discontinue abruptly, dose must be gradually reduced • Start medication at bedtime as it can cause drowsiness and dizziness 	<ul style="list-style-type: none"> • May be beneficial in clients with co-morbid ADHD or insomnia • Weekly patch may improve adherence • Relatively expensive 	<ul style="list-style-type: none"> • Can be poorly tolerated due to side effects • Drug interaction and disease states may limit use

^NRT dosing is based on recommendations from package inserts. Clients can safely smoke and continue to use NRT beyond package instructions. We recommend using NRT until the client feels ready to step down therapy or stop treatment with minimal risk for relapse.

APPENDIX 4: TOBACCO USE DISORDER MEDICATION PHARMACOTHERAPY SELECTION

Level of Recommendation	Medication(s)	Pertinent Treatment Considerations (Not exhaustive, see Appendix 3 for additional details)
Strongest	Varenicline	1) Shown to be most efficacious in general and MH populations compared to other monotherapy pharmacologic treatments
	NRT combination: nicotine patch + gum or lozenge	2) Cost-effective 3) Has history of demonstrating superior efficacy over other monotherapy pharmacologic treatments 4) Produces relatively constant levels of nicotine and allows for acute dose titration as needed
Moderate	NRT monotherapy: nicotine patch, gum, or lozenge	5) NRT monotherapy results in significantly lower quit rates than combination NRT 6) If a single NRT agent is preferred, the patch has been shown to be most efficacious.
	Bupropion	7) Least robust effects compared to other pharmacologic treatments 8) Treatment for co-morbid depression 9) Drug interactions, precautions, and contraindications may preclude use in clients with mental health disorders
Lowest	Nortriptyline	10) Moderate efficacy in clients who cannot use a first-line agent or who need an adjunct to first-line therapy 11) Treatment of co-morbid depression, chronic pain, insomnia, and anxiety 12) High side effect burden 13) Dangerous in overdose
	Clonidine	14) Treatment of comorbid ADHD 15) Limited evidence of benefit over placebo

APPENDIX 5: NOTABLE DRUG INTERACTIONS OF PSYCHIATRIC MEDICATIONS WITH HYDROCARBONS FROM TOBACCO SMOKE

Drug/Class	Mechanism of interaction and effects
Alprazolam	Conflicting data on significance, but possible ↓ plasma concentrations (up to 50%); ↓ half-life (35%).
Caffeine	Metabolism (induction of CYP1A2); ↑ clearance (56%). Caffeine levels likely ↑ after cessation
Chlorpromazine	↓ AUC (36%) and serum concentrations (24%). ↓ Sedation and hypotension possible in smokers; smokers may require ↑ dosages.
Clozapine	↑ Metabolism (induction of CYP1A2); ↓ plasma concentrations (by 18%). ↑ Levels upon cessation may occur; closely monitor drug levels and reduce dose as required to avoid toxicity.
Fluvoxamine	↑ Metabolism (induction of CYP1A2); ↑ clearance (24%); ↓ AUC (31%); ↓ Cmax (32%) and C _{ss} (39%). Dosage modifications not routinely recommended but smokers may need ↑ dosages.
Haloperidol	↑ Clearance (44%); ↓ serum concentrations (70%); data are inconsistent therefore clinical significance is not established
Methadone	Possible ↑ metabolism (induction of CYP1A2, a minor pathway for methadone). Carefully monitor response upon cessation.
Olanzapine	↑ Metabolism (induction of CYP1A2); ↑ clearance (98%); ↓ serum concentrations (2%). Dosage modifications not routinely recommended but smokers may need ↑ dosages.
Propranolol	↑ Clearance (77%; via side-chain oxidation and glucuronidation).
Ropinirole	↓ Cmax (30%) and AUC (38%) in study with clients with restless legs syndrome. Smokers may need ↑ dosages.
Tizanidine	↓ AUC (30–40%) and ↓ half-life (10%) observed in male smokers.
Tricyclic antidepressants (e.g. imipramine, nortriptyline)	Possible interaction with tricyclic antidepressants in the direction of ↓ blood levels, but the clinical significance is not established.

Not a comprehensive list, for additional interactions see:

<https://smokingcessationleadership.ucsf.edu/sites/smokingcessationleadership.ucsf.edu/files/A4%20DI%20TABLE.pdf>