

STEP One: ASK about Tobacco Use

➔ Suggested Dialogue

- ✓ Do you ever smoke or use any type of tobacco?
 - I take time to talk with all of my patients about tobacco use—because it's important.
- ✓ Condition X often is caused or worsened by exposure to tobacco smoke. Do you, or does someone in your household smoke?
- ✓ Medication X often is used for conditions linked with or caused by smoking. Do you, or does someone in your household smoke?

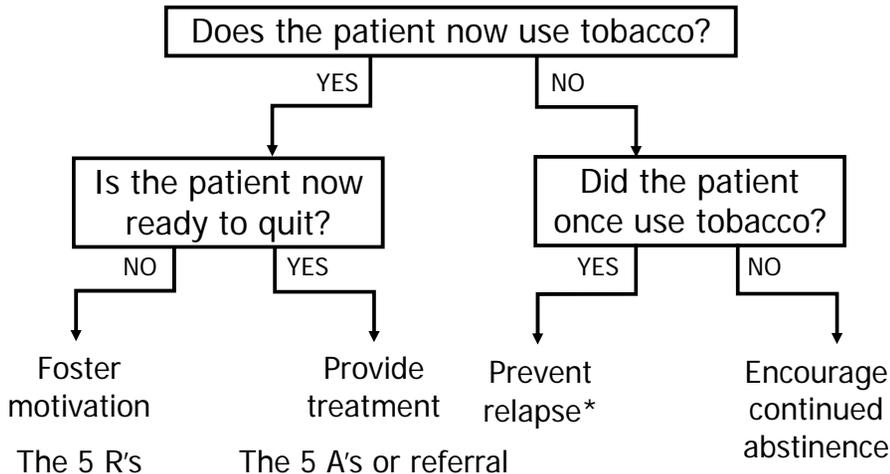
STEP Two: ADVISE to Quit

➔ Suggested Dialogue

- Quitting is the most important thing you can do to protect your health now and in the future. I have training to help my patients quit, and when you are ready I would be more than happy to work with you to design a treatment plan.
- What are your thoughts about quitting? Might you consider quitting sometime in the next month?

Prior to imparting advice, consider asking the patient for permission to do so – e.g., “May I tell you why this concerns me?” [then elaborate on patient-specific concerns]

STEP Three: ASSESS Readiness to Quit



* Relapse prevention interventions are not necessary if patient has not used tobacco for many years and is not at risk for re-initiation.

Fiore MC, Jaén CR, Baker TB, et al. *Treating Tobacco Use and Dependence: 2008 Update*. Clinical Practice Guideline. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service. May 2008.

STEP Four: ASSIST with Quitting



✓ Assess Tobacco Use History

- Current use: type(s) of tobacco used, amount
- Past use:
 - Duration of tobacco use
 - Changes in levels of use recently
- Past quit attempts:
 - Number of attempts, date of most recent attempt, duration
 - Methods used previously—What did or didn't work? Why or why not?
 - Prior medication administration, dose, compliance, duration of treatment
 - Reasons for relapse

✓ Discuss Key Issues (for the upcoming or current quit attempt)

- Reasons/motivation for wanting to quit (or avoid relapse)
- Confidence in ability to quit (or avoid relapse)
- Triggers for tobacco use
- Routines and situations associated with tobacco use
- Stress-related tobacco use
- Concerns about weight gain
- Concerns about withdrawal symptoms

✓ Facilitate Quitting Process

- Discuss methods for quitting: pros and cons of the different methods
- Set a quit date: ideally, less than 2 weeks away
- Recommend Tobacco Use Log
- Discuss coping strategies (cognitive, behavioral)
- Discuss withdrawal symptoms
- Discuss concept of “slip” versus relapse
- Provide medication counseling: compliance, proper use, with demonstration
- Offer to assist throughout the quit attempt

✓ Evaluate the Quit Attempt (at follow-up)

- Status of attempt
- “Slips” and relapse
- Medication compliance and plans for discontinuation

STEP Five: ARRANGE Follow-up Counseling

- ✓ Monitor patients' progress throughout the quit attempt. Follow-up contact should occur during the first week after quitting. A second follow-up contact is recommended in the first month. Additional contacts should be scheduled as needed. Counseling contacts can occur face-to-face, by telephone, or by e-mail. Keep patient progress notes.
- ✓ Address temptations and triggers; discuss strategies to prevent relapse.
- ✓ Congratulate patients for continued success.



DRUG INTERACTIONS WITH TOBACCO SMOKE

Many interactions between tobacco smoke and medications have been identified. Note that in most cases it is the tobacco smoke—not the nicotine—that causes these drug interactions. Tobacco smoke interacts with medications through pharmacokinetic (PK) and pharmacodynamic (PD) mechanisms. PK interactions affect the absorption, distribution, metabolism, or elimination of other drugs, potentially causing an altered pharmacologic response. The majority of PK interactions with smoking are the result of induction of hepatic cytochrome P450 enzymes (primarily CYP1A2). PD interactions alter the expected response or actions of other drugs. The amount of tobacco smoking needed to have an effect has not been established, and the assumption is that any smoker is susceptible to the same degree of interaction. The most clinically significant interactions are depicted in the shaded rows.

DRUG/CLASS	MECHANISM OF INTERACTION AND EFFECTS
Pharmacokinetic Interactions	
Alprazolam (Xanax)	<ul style="list-style-type: none"> Conflicting data on significance, but possible ↓ plasma concentrations (up to 50%); ↓ half-life (35%).
Bendamustine (Treanda)	<ul style="list-style-type: none"> Metabolized by CYP1A2. Manufacturer recommends using with caution in smokers due to likely ↓ bendamustine concentrations, with ↑ concentrations of its two active metabolites.
Caffeine	<ul style="list-style-type: none"> ↑ Metabolism (induction of CYP1A2); ↑ clearance (56%). Caffeine levels likely ↑ after cessation.
Chlorpromazine (Thorazine)	<ul style="list-style-type: none"> ↓ Area under the curve (AUC) (36%) and serum concentrations (24%). ↓ Sedation and hypotension possible in smokers; smokers may require ↑ dosages.
Clopidogrel (Plavix)	<ul style="list-style-type: none"> ↑ Metabolism (induction of CYP1A2) of clopidogrel to its active metabolite. Clopidogrel's effects are enhanced in smokers (≥10 cigarettes/day): significant ↑ platelet inhibition, ↓ platelet aggregation; while improved clinical outcomes have been shown, may also ↑ risk of bleeding.
Clozapine (Clozaril)	<ul style="list-style-type: none"> ↑ Metabolism (induction of CYP1A2); ↓ plasma concentrations (18%). ↑ Levels upon cessation may occur; closely monitor drug levels and reduce dose as required to avoid toxicity.
Erlotinib (Tarceva)	<ul style="list-style-type: none"> ↑ Clearance (24%); ↓ trough serum concentrations (2-fold).
Flecainide (Tambacor)	<ul style="list-style-type: none"> ↑ Clearance (61%); ↓ trough serum concentrations (25%). Smokers may need ↑ dosages.
Fluvoxamine (Luvox)	<ul style="list-style-type: none"> ↑ Metabolism (induction of CYP1A2); ↑ clearance (24%); ↓ AUC (31%); ↓ plasma concentrations (32%). Dosage modifications not routinely recommended but smokers may need ↑ dosages.
Haloperidol (Haldol)	<ul style="list-style-type: none"> ↑ Clearance (44%); ↓ serum concentrations (70%).
Heparin	<ul style="list-style-type: none"> Mechanism unknown but ↑ clearance and ↓ half-life are observed. Smoking has prothrombotic effects. Smokers may need ↑ dosages due to PK and PD interactions.
Insulin, subcutaneous	<ul style="list-style-type: none"> Possible ↓ insulin absorption secondary to peripheral vasoconstriction; smoking may cause release of endogenous substances that cause insulin resistance. PK & PD interactions likely not clinically significant; smokers may need ↑ dosages.
Irinotecan (Camptosar)	<ul style="list-style-type: none"> ↑ Clearance (18%); ↓ serum concentrations of active metabolite, SN-38 (~40%; via induction of glucuronidation); ↓ systemic exposure resulting in lower hematologic toxicity and may reduce efficacy. Smokers may need ↑ dosages.
Mexiletine (Mexitol)	<ul style="list-style-type: none"> ↑ Clearance (25%; via oxidation and glucuronidation); ↓ half-life (36%).
Olanzapine (Zyprexa)	<ul style="list-style-type: none"> ↑ Metabolism (induction of CYP1A2); ↑ clearance (98%); ↓ serum concentrations (12%). Dosage modifications not routinely recommended but smokers may need ↑ dosages.
Propranolol (Inderal)	<ul style="list-style-type: none"> ↑ Clearance (77%; via side-chain oxidation and glucuronidation).
Ropinirole (Requip)	<ul style="list-style-type: none"> ↓ C_{max} (30%) and AUC (38%) in study with patients with restless legs syndrome. Smokers may need ↑ dosages.
Tacrine (Cognex)	<ul style="list-style-type: none"> ↑ Metabolism (induction of CYP1A2); ↓ half-life (50%); serum concentrations 3-fold lower. Smokers may need ↑ dosages.
Theophylline (Theo Dur, etc.)	<ul style="list-style-type: none"> ↑ Metabolism (induction of CYP1A2); ↑ clearance (58–100%); ↓ half-life (63%). Levels should be monitored if smoking is initiated, discontinued, or changed. Maintenance doses are considerably higher in smokers. ↑ Clearance with second-hand smoke exposure.
Tricyclic antidepressants (e.g., imipramine, nortriptyline)	<ul style="list-style-type: none"> Possible interaction with tricyclic antidepressants in the direction of ↓ blood levels, but the clinical significance is not established.
Tizanidine (Zanaflex)	<ul style="list-style-type: none"> ↓ AUC (30–40%) and ↓ half-life (10%) observed in male smokers.
Warfarin	<ul style="list-style-type: none"> ↑ Metabolism (induction of CYP1A2) of R-enantiomer; however, S-enantiomer is more potent and effect on INR is inconclusive. Consider monitoring INR upon smoking cessation.
Pharmacodynamic Interactions	
Benzodiazepines (diazepam, chlordiazepoxide)	<ul style="list-style-type: none"> ↓ Sedation and drowsiness, possibly caused by nicotine stimulation of central nervous system.
Beta-blockers	<ul style="list-style-type: none"> Less effective antihypertensive and heart rate control effects; possibly caused by nicotine-mediated sympathetic activation. Smokers may need ↑ dosages.
Corticosteroids, inhaled	<ul style="list-style-type: none"> Smokers with asthma may have less of a response to inhaled corticosteroids.
Hormonal contraceptives	<ul style="list-style-type: none"> ↑ Risk of cardiovascular adverse effects (e.g., stroke, myocardial infarction, thromboembolism) in women who smoke and use oral contraceptives. Ortho Evra patch users shown to have 2-fold ↑ risk of venous thromboembolism compared to oral contraceptive users, likely due to ↑ estrogen exposure (60% higher levels). ↑ Risk with age and with heavy smoking (≥15 cigarettes per day) and is quite marked in women ≥35 years old.
Opioids (propoxyphene, pentazocine)	<ul style="list-style-type: none"> ↓ Analgesic effect; smoking may ↑ the metabolism of propoxyphene (15–20%) and pentazocine (40%). Mechanism unknown. Smokers may need ↑ opioid dosages for pain relief.

Adapted and updated, from Zevin S, Benowitz NL. Drug interactions with tobacco smoking. *Clin Pharmacokinet* 1999;36:425–438.



COPING WITH QUITTING: COGNITIVE AND BEHAVIORAL STRATEGIES

<p>COGNITIVE STRATEGIES focus on <i>retraining the way a patient thinks</i>. Often, patients mentally deliberate on the fact that they are thinking about a cigarette, and this leads to relapse. Patients must recognize that thinking about a cigarette doesn't mean they need to have one.</p>	
REVIEW COMMITMENT TO QUIT	Each morning, say, "I am proud that I made it through another day without tobacco!" Remind oneself that cravings and temptations are temporary and will pass. Announce, either silently or aloud, "I am a nonsmoker, and the temptation will pass."
DISTRACTIVE THINKING	Use deliberate, immediate refocusing of thinking toward other thoughts when cued by thoughts about tobacco use.
POSITIVE SELF-TALKS, PEP TALKS	Say, "I can do this," and remind oneself of previous difficult situations in which tobacco use was avoided.
RELAXATION THROUGH IMAGERY	Center mind toward positive, relaxing thoughts.
MENTAL REHEARSAL, VISUALIZATION	Prepare for situations that might arise by envisioning how best to handle them. For example, envision what would happen if offered a cigarette by a friend—mentally craft and rehearse a response, and perhaps even practice it by saying it aloud.
<p>BEHAVIORAL STRATEGIES involve <i>specific actions to reduce risk for relapse</i>. These strategies should be considered prior to quitting, after determining patient-specific triggers and routines or situations associated with tobacco use. Below are strategies for several of the more common cues or causes for relapse.</p>	
STRESS	Anticipate upcoming challenges at work, at school, or in personal life. Develop a substitute plan for tobacco use during times of stress (e.g., use deep breathing, take a break or leave the situation, call a supportive friend or family member, perform self-massage, use nicotine replacement therapy).
ALCOHOL	<i>Drinking alcohol can lead to relapse.</i> Consider limiting or abstaining from alcohol during the early stages of quitting.
OTHER TOBACCO USERS	<i>Quitting is more difficult if the patient is around other tobacco users. This is especially difficult if another tobacco user is in the household.</i> During the early stages of quitting, limit prolonged contact with individuals who are using tobacco. Ask co-workers, friends, and housemates not to smoke or use tobacco in your presence.
ORAL GRATIFICATION NEEDS	Have nontobacco oral substitutes (e.g., gum, sugarless candy, straws, toothpicks, lip balm, toothbrush, nicotine replacement therapy, bottled water) readily available.
AUTOMATIC SMOKING ROUTINES	Anticipate routines associated with tobacco use and develop an alternative plan. Examples: MORNING COFFEE: change morning routine, drink tea instead of coffee, take shower before drinking coffee, take a brisk walk shortly after awakening. WHILE DRIVING: remove all tobacco from car, have car interior detailed, listen to a book on tape or talk radio, use oral substitute. WHILE ON THE PHONE: stand while talking, limit call duration, change phone location, keep hands occupied by doodling or sketching. AFTER MEALS: get up and immediately do dishes or take a brisk walk after eating, call supportive friend.
POSTCESSATION WEIGHT GAIN	Do not attempt to modify multiple behaviors at one time. If weight gain is a barrier to quitting, engage in regular physical activity and adhere to a healthful diet (as opposed to strict dieting). Carefully plan and prepare meals, increase fruit and water intake to create a feeling of fullness, and chew sugarless gum or eat sugarless candies. Consider use of pharmacotherapy shown to delay weight gain (e.g., nicotine gum, nicotine lozenge, bupropion).
CRAVINGS FOR TOBACCO	Cravings for tobacco are temporary and usually pass within 5–10 minutes. Handle cravings through distractive thinking, take a break, do something else, take deep breaths, perform self-massage.



PHARMACOLOGIC PRODUCT GUIDE: FDA-APPROVED MEDICATIONS FOR SMOKING CESSATION

		NICOTINE REPLACEMENT THERAPY (NRT) FORMULATIONS				BUPROPION SR	VARENICLINE
		GUM	LOZENGE	TRANSDERMAL PATCH	NASAL SPRAY	ORAL INHALER	
PRODUCT	Nicorette ¹ , Generic OTC 2 mg, 4 mg original, cinnamon, fruit, mint, orange	Nicorette Lozenge, ¹ Nicorette Mini Lozenge, ¹ Generic OTC 2 mg, 4 mg cherry, mint	NicoDerm CO ¹ , Generic OTC (NicoDerm CO, generic) Rx (generic) 7 mg, 14 mg, 21 mg (24-hour release)	Nicotrol NS ² Rx Metered spray 0.5 mg nicotine in 50 mL aqueous nicotine solution	Nicotrol Inhaler ² Rx 10 mg cartridge delivers 4 mg inhaled nicotine vapor	Zyban ¹ , Generic Rx 150 mg sustained-release tablet	Chantix ² Rx 0.5 mg, 1 mg tablet
PRECAUTIONS	<ul style="list-style-type: none"> Recent (≤ 2 weeks) myocardial infarction Serious underlying arrhythmias Serious or worsening angina pectoris Temporomandibular joint disease Pregnancy³ and breastfeeding Adolescents (<18 years) 	<ul style="list-style-type: none"> Recent (≤ 2 weeks) myocardial infarction Serious underlying arrhythmias Serious or worsening angina pectoris Pregnancy³ and breastfeeding Adolescents (<18 years) 	<ul style="list-style-type: none"> Recent (≤ 2 weeks) myocardial infarction Serious underlying arrhythmias Serious or worsening angina pectoris Pregnancy³ (Rx formulations, category D) and breastfeeding Adolescents (<18 years) 	<ul style="list-style-type: none"> Recent (≤ 2 weeks) myocardial infarction Serious underlying arrhythmias Serious or worsening angina pectoris Underlying chronic nasal disorders (rhinitis, nasal polyps, sinusitis) Severe reactive airway disease Pregnancy³ (category D) and breastfeeding Adolescents (<18 years) 	<ul style="list-style-type: none"> Recent (≤ 2 weeks) myocardial infarction Serious underlying arrhythmias Serious or worsening angina pectoris Bronchospastic disease Pregnancy³ (category D) and breastfeeding Adolescents (<18 years) 	<ul style="list-style-type: none"> Concomitant therapy with medications or medical conditions known to lower the seizure threshold Severe hepatic cirrhosis Pregnancy³ (category C) and breastfeeding Adolescents (<18 years) <p>Warning:</p> <ul style="list-style-type: none"> BLACK-BOXED WARNING for neuropsychiatric symptoms⁴ <p>Contraindications:</p> <ul style="list-style-type: none"> Seizure disorder Concomitant bupropion (e.g., Wellbutrin) therapy Current or prior diagnosis of bulimia or anorexia nervosa Simultaneous abrupt discontinuation of alcohol or sedatives/benzodiazepines MAO inhibitor therapy in previous 14 days 	<ul style="list-style-type: none"> Severe renal impairment (dosage adjustment is necessary) Pregnancy³ (category C) and breastfeeding Adolescents (<18 years) <p>Warnings:</p> <ul style="list-style-type: none"> BLACK-BOXED WARNING for neuropsychiatric symptoms⁴ Cardiovascular adverse events in patients with existing cardiovascular disease
DOSING	<p>1st cigarette ≤30 minutes after waking: 4 mg</p> <p>1st cigarette >30 minutes after waking: 2 mg</p> <p>Weeks 1–6: 1 piece q 1–2 hours</p> <p>Weeks 7–9: 1 piece q 2–4 hours</p> <p>Weeks 10–12: 1 piece q 4–8 hours</p> <ul style="list-style-type: none"> Maximum, 24 pieces/day 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 No food or beverages 15 minutes before or during use Duration: up to 12 weeks 	<p>1st cigarette ≤30 minutes after waking: 4 mg</p> <p>1st cigarette >30 minutes after waking: 2 mg</p> <p>Weeks 1–6: 1 lozenge q 1–2 hours</p> <p>Weeks 7–9: 1 lozenge q 2–4 hours</p> <p>Weeks 10–12: 1 lozenge q 4–8 hours</p> <ul style="list-style-type: none"> Maximum, 20 lozenges/day Allow to dissolve slowly (20–30 minutes for standard; 10 minutes for mini) 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 Duration: up to 12 weeks 	<p>>10 cigarettes/day: 21 mg/day x 4 weeks (generic) 6 weeks (NicoDerm CO)</p> <p>14 mg/day x 2 weeks 7 mg/day x 2 weeks</p> <p>≤10 cigarettes/day: 14 mg/day x 6 weeks 7 mg/day x 2 weeks</p> <ul style="list-style-type: none"> May wear patch for 16 hours if patient experiences sleep disturbances (remove at bedtime) Duration: 8–10 weeks 	<p>1–2 doses/hour (8–40 doses/day) One dose = 2 sprays (one in each nostril); each spray delivers 0.5 mg of nicotine to the nasal mucosa</p> <ul style="list-style-type: none"> Maximum <ul style="list-style-type: none"> – 5 doses/hour or – 40 doses/day For best results, initially use at least 8 doses/day Do not sniff, swallow, or inhale through the nose as the spray is being administered Duration: 3–6 months 	<p>6–16 cartridges/day Individualize dosing; initially use 1 cartridge q 1–2 hours</p> <ul style="list-style-type: none"> Best effects with continuous puffing for 20 minutes Initially use at least 6 cartridges/day Nicotine in cartridge is depleted after 20 minutes of active puffing Inhale into back of throat or puff in short breaths Do NOT inhale into the lungs (like a cigarette) but “puff” as if lighting a pipe Open cartridge retains potency for 24 hours No food or beverages 15 minutes before or during use Duration: 3–6 months 	<p>150 mg po q AM x 3 days, then 150 mg po bid</p> <ul style="list-style-type: none"> Do not exceed 300 mg/day Begin therapy 1–2 weeks prior to quit date Allow at least 8 hours between doses Avoid bedtime dosing to minimize insomnia Dose tapering is not necessary Can be used safely with NRT Duration: 7–12 weeks, with maintenance up to 6 months in selected patients 	<p>Days 1–3: 0.5 mg po q AM</p> <p>Days 4–7: 0.5 mg po bid</p> <p>Weeks 2–12: 1 mg po bid</p> <ul style="list-style-type: none"> Begin therapy 1 week prior to quit date; alternatively, the patient can begin therapy and then quit smoking between days 8–35 of treatment Take dose after eating and with a full glass of water Dose tapering is not necessary Dosing adjustment is necessary for patients with severe renal impairment Duration: 12 weeks; an additional 12-week course may be used in selected patients

NICOTINE REPLACEMENT THERAPY (NRT) FORMULATIONS							
	GUM	LOZENGE	TRANSDERMAL PATCH	NASAL SPRAY	ORAL INHALER	BUPROPION SR	VARENICLINE
ADVERSE EFFECTS	<ul style="list-style-type: none"> ▪ Mouth/jaw soreness ▪ Hiccups ▪ Dyspepsia ▪ Hypersalivation ▪ Effects associated with incorrect chewing technique: <ul style="list-style-type: none"> – Lightheadedness – Nausea/vomiting – Throat and mouth irritation 	<ul style="list-style-type: none"> ▪ Nausea ▪ Hiccups ▪ Cough ▪ Heartburn ▪ Headache ▪ Flatulence ▪ Insomnia 	<ul style="list-style-type: none"> ▪ Local skin reactions (erythema, pruritus, burning) ▪ Headache ▪ Sleep disturbances (insomnia, abnormal/vivid dreams); associated with nocturnal nicotine absorption 	<ul style="list-style-type: none"> ▪ Nasal and/or throat irritation (hot, peppery, or burning sensation) ▪ Rhinitis ▪ Tearing ▪ Sneezing ▪ Cough ▪ Headache 	<ul style="list-style-type: none"> ▪ Mouth and/or throat irritation ▪ Cough ▪ Headache ▪ Rhinitis ▪ Dyspepsia ▪ Hiccups 	<ul style="list-style-type: none"> ▪ Insomnia ▪ Dry mouth ▪ Nervousness/difficulty concentrating ▪ Rash ▪ Constipation ▪ Seizures (risk is 0.1%) ▪ Neuropsychiatric symptoms (rare; see PRECAUTIONS) 	<ul style="list-style-type: none"> ▪ Nausea ▪ Sleep disturbances (insomnia, abnormal/vivid dreams) ▪ Constipation ▪ Flatulence ▪ Vomiting ▪ Neuropsychiatric symptoms (rare; see PRECAUTIONS)
ADVANTAGES	<ul style="list-style-type: none"> ▪ Might satisfy oral cravings ▪ Might delay weight gain ▪ Patients can titrate therapy to manage withdrawal symptoms ▪ Variety of flavors are available 	<ul style="list-style-type: none"> ▪ Might satisfy oral cravings ▪ Might delay weight gain ▪ Easy to use and conceal ▪ Patients can titrate therapy to manage withdrawal symptoms ▪ Variety of flavors are available 	<ul style="list-style-type: none"> ▪ Provides consistent nicotine levels over 24 hours ▪ Easy to use and conceal ▪ Once daily dosing associated with fewer compliance problems 	<ul style="list-style-type: none"> ▪ Patients can titrate therapy to rapidly manage withdrawal symptoms 	<ul style="list-style-type: none"> ▪ Patients can titrate therapy to manage withdrawal symptoms ▪ Mimics hand-to-mouth ritual of smoking (could also be perceived as a disadvantage) 	<ul style="list-style-type: none"> ▪ Easy to use; oral formulation might be associated with fewer compliance problems ▪ Might delay weight gain ▪ Can be used with NRT ▪ Might be beneficial in patients with depression 	<ul style="list-style-type: none"> ▪ Easy to use; oral formulation might be associated with fewer compliance problems ▪ Offers a new mechanism of action for patients who have failed other agents
DISADVANTAGES	<ul style="list-style-type: none"> ▪ Need for frequent dosing can compromise compliance ▪ Might be problematic for patients with significant dental work ▪ Patients must use proper chewing technique to minimize adverse effects ▪ Gum chewing may not be socially acceptable 	<ul style="list-style-type: none"> ▪ Need for frequent dosing can compromise compliance ▪ Gastrointestinal side effects (nausea, hiccups, heartburn) might be bothersome 	<ul style="list-style-type: none"> ▪ Patients cannot titrate the dose to acutely manage withdrawal symptoms ▪ Allergic reactions to adhesive might occur ▪ Patients with dermatologic conditions should not use the patch 	<ul style="list-style-type: none"> ▪ Need for frequent dosing can compromise compliance ▪ Nasal/throat irritation may be bothersome ▪ Patients must wait 5 minutes before driving or operating heavy machinery ▪ Patients with chronic nasal disorders or severe reactive airway disease should not use the spray 	<ul style="list-style-type: none"> ▪ Need for frequent dosing can compromise compliance ▪ Initial throat or mouth irritation can be bothersome ▪ Cartridges should not be stored in very warm conditions or used in very cold conditions ▪ Patients with underlying bronchospastic disease must use with caution 	<ul style="list-style-type: none"> ▪ Seizure risk is increased ▪ Several contraindications and precautions preclude use in some patients (see PRECAUTIONS) ▪ Patients should be monitored for potential neuropsychiatric symptoms⁴ (see PRECAUTIONS) 	<ul style="list-style-type: none"> ▪ May induce nausea in up to one third of patients ▪ Patients should be monitored for potential neuropsychiatric symptoms⁴ (see PRECAUTIONS)
COST/DAY ⁵	2 mg or 4 mg: \$2.25–\$4.41 (9 pieces)	2 mg or 4 mg: \$2.61–\$4.95 (9 pieces)	\$1.87–\$3.52 (1 patch)	\$4.43 (8 doses)	\$7.68 (6 cartridges)	\$3.62–\$7.46 (2 tablets)	\$5.38–\$6.20 (2 tablets)

¹ Marketed by GlaxoSmithKline.

² Marketed by Pfizer.

³ The U.S. Clinical Practice Guideline states that pregnant smokers should be encouraged to quit without medication based on insufficient evidence of effectiveness and theoretical concerns with safety. Pregnant smokers should be offered behavioral counseling interventions that exceed minimal advice to quit.

⁴ In July 2009, the FDA mandated that the prescribing information for all bupropion- and varenicline-containing products include a black-boxed warning highlighting the risk of serious neuropsychiatric symptoms, including changes in behavior, hostility, agitation, depressed mood, suicidal thoughts and behavior, and attempted suicide. Clinicians should advise patients to stop taking varenicline or bupropion SR and contact a healthcare provider immediately if they experience agitation, depressed mood, and any changes in behavior that are not typical of nicotine withdrawal, or if they experience suicidal thoughts or behavior. If treatment is stopped due to neuropsychiatric symptoms, patients should be monitored until the symptoms resolve.

⁵ Average wholesale price from Medi-Span Electronic Drug File. Indianapolis, IN: Wolters Kluwer Health, July 2011.

Abbreviations: MAO, monoamine oxidase; NRT, nicotine replacement therapy; OTC, over-the-counter (non-prescription product); Rx, prescription product.

For complete prescribing information, please refer to the manufacturers' package inserts.