OVERVIEW

Despite the fact that tobacco use is the primary preventable cause of disease and death in the United States, approximately one quarter of American adults smoke. Smoking has a causal or contributory role in the development of a variety of medical conditions (Table 1), with lung and cardiovascular diseases being the most prevalent. Exposure to secondhand smoke predisposes infants and children to sudden infant death syndrome, respiratory infections, asthma, and otitis media.

Most smokers begin during adolescence, typically by the age of 16. One third of these individuals will eventually die of a tobacco-related disease. Among adolescents, smoking has risen dramatically since 1990, with close to 3,000 children and adolescents becoming regular tobacco users each day. An estimated 47 million Americans smoke; 70% want to quit.

Approaches to Treatment

Compared to two decades ago, tobacco users are now able to select from many treatment options for quitting. An analysis of over 6,000 published articles has revealed two clear treatment-related themes: 1) the use of approved medications for cessation at least doubles the likelihood of quitting, and 2) the effects of medications are substantially increased when coupled with behavioral interventions. Behavioral interventions include, but are not limited to, counseling from a pharmacist or other health professional.

Given that medications for cessation are available primarily through pharmacies and several are nonprescription products, pharmacists are in a unique position to help patients with quitting. In fact, research indicates that pharmacists have a positive effect on the cessation rates of patients. Furthermore, consultation with a pharmacist has been shown to be an important and cost-beneficial component of smoking cessation treatment. Pharmacists can take an active role in tobacco control efforts by identifying tobacco users, advising them to quit, and facilitating quit attempts.

Facts For Patients

- Cigarette smoking is the single most preventable cause of premature death in the United States. Each year, more than 430,000 Americans die from smoking-related illnesses. One in every five deaths in the United States is smoking related.
- Smoking-related illnesses cost the United States more than $50 billion dollars each year.
- Effective medications are available to help patients quit smoking. Unless there are contraindications, all patients who are trying to quit should use one or more approved medications. Drug therapy should be combined with behavioral counseling to further increase patients’ chances for success.
- FDA-approved first-line medications for smoking cessation include the nicotine patch, nicotine gum, nicotine nasal spray, nicotine inhaler, and sustained release bupropion. Second-line medications, which are not approved for smoking cessation but have demonstrated some effectiveness include clonidine and nortriptyline.
- It is never too late to quit. Quitting, at any age, is associated with significant health benefits, including improved lung function, reduced risk of developing lung and other tobacco-related cancers, and a reduced risk of coronary heart disease.

Continuing Education Objectives

- Apply the Five “A”s (Ask, Advise, Assess, Assist, Arrange) in promoting smoking cessation with patients.
- State patient selection characteristics, dosing and adverse effects for the five FDA-approved medications for smoking cessation.
- Integrate behavioral counseling and instruction on the use of approved medications for smoking cessation.
Nicotine Polacrilex Gum
• Chew the gum slowly. At the first sign of a peppery taste or tingle (usually requires 15-30 chews), park the gum between the cheek and gum. Chew again when the taste or tingle fades. Repeat until the peppery taste or tingle doesn’t return, generally about 30 minutes.
• Avoid food and acidic beverages (coffee, juices, wine, soft drinks) 15 minutes before and while chewing the gum.
• Chew the gum on a fixed schedule (1 piece every 1-2 hours, initially) rather than "as needed," tapering downward throughout the recommended 3-month treatment period. Do not chew more than 24 pieces per day.

Transdermal Nicotine Patch
• Each morning, apply to a hairless, low-friction area of the skin, generally between the neck and waist. Press firmly on the patch with the palm of the hand for 10 seconds. Rotate application sites each day.
• Water will not harm patches that are applied correctly.
• Mild skin irritation may occur at the patch site; this typically disappears in a day or two. If skin stays red for more than 4 days or if swelling or a rash appears, notify your pharmacist or physician.
• If you have vivid dreams or difficulty sleeping, remove the (24-hour) patch at bedtime.

Nicotine Nasal Spray
• Prior to first use, prime the pump into a tissue until a fine spray is observed (6-8 pumps). If the pump is not used within 24 hours, prime 1-2 times into a tissue.
• Blow the nose, tilt the head back slightly, and insert tip of bottle as far into nose as is comfortable. Breathe in through mouth and press bottom of bottle to spray. Do not sniff or inhale while spraying. Breathe out through the mouth. Repeat for other nostril. If the nose runs, sniff gently. Wait 2-3 minutes before blowing the nose. Do not use more than 5 times per hour or 40 times per day.
• Side effects should lessen over a few days. Because the spray can cause tearing or sneezing, avoid driving or operating heavy machinery within 5 minutes of use.

Nicotine Inhaler
• To open, align marks on the mouthpiece and pull off the top. Press a nicotine cartridge firmly into the bottom of the mouthpiece until the seal breaks. Replace the top; press down firmly to break the top seal of the cartridge. Twist to misalign marks.
• Inhalate into back of throat or puff in short breaths, as if lighting a pipe.
• Each cartridge lasts about 80 puffs, which is about 20 minutes of active puffing. The inhaler can be used for a few minutes, put down, and used again later. However, once opened, each cartridge (whether fully used or not) should be replaced after 24 hrs.

• Store cartridges at room temperature (below 86°F). Cartridges should not be used at temperatures below 59°F.
• Avoid food and acidic beverages 15 minutes before and while using the inhaler.

Bupropion SR
• Begin by taking one tablet (150mg) once a day for 3 days; if tolerated increase to 150mg twice a day (at least 8 hours apart) on day four. If insomnia is experienced, avoid taking the second dose close to bedtime.
• It is OK to continue smoking until the quit date, which should be during the second week of treatment.
• About 1 in 1000 patients experience seizures. Discuss your seizure risk with a physician before starting therapy.

Figure 1. Assessing Readiness to Quit

Table 1. Smoking-Related Diseases

- Cardiovascular disease
  chronic conditions accelerated by smoking: coronary heart disease, cerebrovascular disease, peripheral vascular disease, aortic aneurysm
  acute events precipitated by smoking: sudden death, myocardial infarction, stroke, reocclusion of coronary or peripheral vessels after graft surgery or angioplasty
- Cancer
  causal role: lung, oral cavity, larynx, esophagus
  contributory role: bladder, kidney, pancreas
  associated with: stomach, cervix
- Chronic obstructive pulmonary disease (COPD) including emphysema and chronic bronchitis
- Pregnancy and perinatal complications (miscarriage/spontaneous abortion, stillbirth, preterm delivery, low birth weight)
- Reduced fertility
- Cataract formation
- Osteoporosis
- Periodontal disease
- Increased risk of middle ear infections, respiratory infections and asthma in children exposed to secondhand smoke
Tobacco Cessation

Tobacco Dependence and Withdrawal

Nicotine is readily absorbed across the respiratory tract epithelium, buccal mucosa (cheek), and skin. The yield of nicotine from one U.S. cigarette is about 1 mg.\textsuperscript{15} After inhalation, nicotine reaches the brain in approximately 10-19 seconds,\textsuperscript{16} resulting in the rapid onset of behaviorally-reinforcing effects on the nervous system, including pleasure, relief of anxiety, improved task performance, improved memory, mood modulation, and skeletal muscle relaxation.\textsuperscript{17} These positive effects, mediated by alterations in neurotransmitter levels, give way to negative withdrawal effects in the absence of nicotine among dependent tobacco users. Withdrawal includes anger, irritability, anxiety, difficulty concentrating, drowsiness, fatigue, hunger/weight gain, impatience, and restlessness.\textsuperscript{18} These symptoms tend to appear in the first 24 hours, peak in the first 1-2 weeks, and generally resolve within 30 days after quitting. Weight gain is usually less than 10 pounds and may be delayed by the use of bupropion or nicotine replacement therapy, particularly nicotine gum. Importantly, many patients report cravings for cigarettes months or years after quitting.

Helping Patients to Quit

According to the Clinical Practice Guideline for Treating Tobacco Use and Dependence,\textsuperscript{9} five key components of counseling are: (1) ask patients whether they use tobacco, (2) advise tobacco users to quit, (3) assess interest in quitting, (4) assist patients with quitting, and (5) arrange follow-up care.\textsuperscript{9,19} (Figure 1.)

Ask: Because smoking interacts with many medications and contributes to the onset and exacerbation of a wide variety of medical conditions, an important element of any drug history and the initial step in providing tobacco cessation treatment is to identify tobacco users. Tobacco use status (current, former, never) and level of use (e.g., number of cigarettes smoked per day) should be documented in the patient profile.

Advise: Pharmacists should strongly advise all tobacco users to quit. The advice should be clear and compelling, yet delivered in a tone conveying concern for the patient’s health and a commitment to help with quitting. Messages should be linked to current health status, medication use, motivation to quit, tobacco’s social and economic costs, and/or the effects of tobacco on others.

Assess: Using the flowchart in Figure 1, a pharmacist quickly can assess a patient’s readiness to quit. This defines the pharmacist’s next course of action, which is providing counseling tailored to the patient’s readiness.

Assist: The focus should be to move patients forward in the process of change, with the ultimate goal being permanent cessation. Because many patients will not be ready to quit, an important part of the “assist” component is helping patients make the decision to quit.

Arrange: Arranging follow-up counseling is an important element of tobacco dependence treatment. Although brief counseling (a recommendation to quit) is effective for some patients, the ability to quit increases when multiple counseling contacts are provided: one or less session(s) leads to a quit rate (at 5 or more months post-cessation) of 12%; 2 to 3 sessions, 4 to 8 sessions, and more than 8 sessions yield estimated quit rates of 16%, 21%, and 25%, respectively. Pharmacists should maintain patient progress records detailing recommendations, treatment methods, dosing regimens, and key dates such as quit dates and tobacco-free anniversaries.

Patients Who Are Ready to Quit

When a patient is ready to quit, the pharmacist should help prepare the patient and design an individualized treatment plan (Table 3). There are two general methods pharmacists can utilize: smoking cessation medications and nondrug therapy. It is estimated that only 3% of smokers are able to quit for a year or more using willpower alone.\textsuperscript{20} Both drug and nondrug therapy improve quit rates, and using these methods in combination yields quit rates higher than those produced by either method alone.\textsuperscript{9} All smokers who are trying to quit should be encouraged to use one or more FDA-approved medications for cessation; potential exceptions include medical contraindications, smoking fewer than 10 cigarettes per day, adolescence, and pregnancy or breast-feeding.\textsuperscript{9} Nondrug methods commonly focus on promoting behavior change. Methods include quitting cold turkey, tapering, self-help materials and formal smoking cessation programs (e.g., face-to-face counseling, telephone counseling, group programs). Massage, acupuncture and hypnosis also are also utilized, although limited data currently exist to support their efficacy.\textsuperscript{9}

Follow-up care can be conducted in person or by telephone, mail, or e-mail. Because most relapses occur within the first 3 months, follow-up should occur soon after the quit date, during the first week. A second follow-up contact is recommended within the first month after quitting and additional contacts should occur periodically. During each contact it is important to congratulate success (if appropriate). Patients should be encouraged to focus on the positive (the ability to refrain from tobacco use) and view slips as a part of the learning experience. Pharmacists should also assess the appropriateness of medication use, ask about side effects, review potential triggers for relapse, elicit the patient’s continued commitment to abstinence, and consider referring the patient for more intensive treatment, if needed.\textsuperscript{9}
Patients Who Are Not Ready to Quit

Motivation for quitting can be enhanced by applying the Five “R”s described below. While it is useful to give patients information about the different methods for quitting, it is not appropriate to prescribe a treatment regimen at this point.

Relevance: Encourage patients to explore their beliefs to identify reasons why quitting is important. Because information has increased impact if it takes on a personal meaning, messages should relate to the patient’s disease status or risk, family or social situation (e.g., having children with asthma), health concerns, age, and other characteristics such as previous quit attempts or barriers to quitting.

Risks: Ask patients to identify negative consequences of their tobacco use, such as acute risks (shortness of breath, harm to the fetus of pregnant women, worsening asthma symptoms), long-term risks (pulmonary disease, cardiovascular disease, cancer), and environmental risks (increased rates of smoking among children, effects of environmental tobacco smoke).

Rewards: Ask patients to identify benefits of quitting; highlight rewards that are most relevant to the patient. Examples are improved health and physical performance, improved taste and smell, reduced spending on cigarettes, reduced risk to others (including fetus/children), reduced aging of skin, and less time wasted smoking.

Roadblocks: Help patients identify barriers to quitting, and assist patients with developing strategies and skills for circumventing each barrier. Common barriers include withdrawal symptoms, fear of failure, weight gain, lack of support, depression, and a sense of loss.

Repetition: Continue to work with patients who have been unable to quit, repeating interventions when possible. Help patients learn from their relapses by exploring reasons for relapse and applying this knowledge in future quit attempts.

Drug Therapy

FDA-approved first-line agents for smoking cessation include four dosage forms of nicot ine replacement therapy (NRT) and sustained-release bupropion. In general, the daily costs of these medications are equal to or less than the daily cost of smoking. (See Table 2.) Drugs that have not received FDA approval for smoking cessation but have been recommended as second-line agents include clonidine and nortriptyline.9

Nicotine Replacement Therapy (NRT)

NRT formulations currently available in the U.S. are the nicotine gum, transdermal patch, nasal spray, and inhaler. Table 2 presents the various products, dosing, adverse effects, advantages, and daily costs of treatment.

The use of NRT approximately doubles the likelihood of quitting compared to placebo.9,21 NRT helps patients with quitting by reducing nicotine withdrawal symptoms while they focus on the behavioral and psychological aspects of smoking. Additionally, because the onset of action for NRT is not as rapid as that of nicotine obtained through smoking, patients become less accustomed to the nearly immediate, reinforcing effects of inhaled tobacco. Prior to beginning NRT, patients must completely stop using all forms of tobacco.

NRT should not be avoided in patients with a history of cardiovascular disease. Caution should be used, however, in the following patient groups: those in the immediate (within 2 weeks) postmyocardial infarction period, those with serious arrhythmias, and those with serious or worsening angina pectoris.7 These concerns are based on the fact that nicotine may cause adverse cardiovascular effects by increasing heart rate and blood pressure. Nicotine also may constrict coronary arteries, leading to cardiac ischemia.22 However, the risks of NRT in patients with cardiovascular disease are small relative to the risks of continued smoking.23,24 Patients with serious underlying cardiovascular disease are advised to use NRT therapy only while under the supervision of a physician.

Other conditions for which NRT should be used with caution include active temporomandibular joint disease (gum only) and pregnancy. Nicotine is classified as pregnancy category D, meaning there is evidence of risk to the human fetus, but the potential benefits of use may outweigh the risks. Because it is assumed that NRT can cause fetal harm, use during pregnancy should be reserved for cases where cessation is not likely to occur with nondrug methods alone and where the increased chance and benefits of cessation outweigh the risks of using NRT. Pregnant women should use NRT only while under physician supervision.

Nicotine Polacrilex Gum

Nicotine polacrilex is a resin complex of nicotine and polacrilin in a sugar free chewing gum base. It is available as 2mg and 4mg strengths, in regular, mint, and orange flavors. The gum contains buffering agents (sodium carbonate, sodium bicarbonate) to increase salivary pH, thereby enhancing absorption of nicotine across the buccal mucosa.

The amount of nicotine absorbed from the 2mg and 4mg gum is variable, but averages 0.9mg and 1.2mg, respectively.25 The nicotine plasma level peaks approximately 30 minutes after chewing a single piece of gum, then the level slowly declines after 2-3 hours. Manufacturers recommend a 12 week course of therapy for the nicotine
Table 2. FDA-approved Nicotine Replacement Therapy Options for Smoking Cessation

<table>
<thead>
<tr>
<th>Products</th>
<th>Dosing</th>
<th>Adverse Effects</th>
<th>Advantages</th>
<th>Cost per Day8</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gum</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Nicorette®</td>
<td>2mg: &lt; 25 cigarettes/day 4mg: &gt; 25 cigarettes/day</td>
<td>mouth/jaw soreness, dyspepsia, hiccups, hypersalivation; effects associated with incorrect chewing technique: light-headedness, nausea/vomiting, throat &amp; mouth irritation, indigestion</td>
<td>• May satisfy oral craving  • May delay weight gain  • Patient can titrate therapy to manage withdrawal symptoms</td>
<td>2 mg: $3.33 - $5.31 (9 pieces)</td>
</tr>
<tr>
<td>(regular, mint, orange)</td>
<td>weeks 1-6: 1 piece q 1-2 hrs weeks 7-9: 1 piece q 2-4 hrs weeks 10-12: 1 piece q 4-8 hrs</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>generic</td>
<td>Not to exceed 24 pieces/day</td>
<td></td>
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<tr>
<td>2mg, 4mg</td>
<td></td>
<td></td>
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<td><strong>Transdermal Preparations</strong></td>
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<tr>
<td>Nicotrol® patch</td>
<td>&gt;10 cigarettes/day: 15 mg x 6 weeks &lt;10 cigarettes/day: NOT recommended</td>
<td>local skin reactions (erythema, pruritus, burning); headache</td>
<td>• One-step process  • Easy to use/conceal  • Fewer compliance issues</td>
<td>$3.68</td>
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<tr>
<td>15 mg (16 hour)</td>
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<tr>
<td>Nicoderm CQ®</td>
<td>&gt;10 cigarettes/day: 21 mg x 6 weeks 14 mg x 2 weeks 7 mg x 2 weeks &lt;10 cigarettes/day: 14 mg x 6 weeks 7 mg x 2 weeks</td>
<td>local skin reactions (erythema, pruritus, burning), headache, sleep disturbances (insomnia) or abnormal dreams (associated with nocturnal nicotine absorption)</td>
<td>• Provides 24 hour steady state concentration, which may reduce morning cravings  • Easy to use/conceal  • Fewer compliance issues  • Generic products that provide 22 mg or 11 mg per 24 hours have the added advantage of a one-step process</td>
<td>$2.53 - $4.07</td>
</tr>
<tr>
<td>21mg, 14mg, 7mg (24 hour)</td>
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<tr>
<td>generic (formerly Habitrol®)</td>
<td>≥10 cigarettes/day: 21 mg x 4 weeks 14 mg x 2 weeks 7 mg x 2 weeks &lt;10 cigarettes/day: 14 mg x 6 weeks 7 mg x 2 weeks</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>21mg, 14mg, 7mg (24 hour)</td>
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<tr>
<td>generic (formerly Prostep®)</td>
<td>&gt; 15 cigarettes/day: 22 mg x 6 weeks ≤15 cigarettes/day: 11 mg x 6 weeks</td>
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<td>22mg, 11mg (24 hour)</td>
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<tr>
<td><strong>Nasal Spray</strong></td>
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<tr>
<td>Nicotrol NS® Metered spray (0.5mg nicotine in 50 µl)</td>
<td>1 to 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) Decrease use over 3-6 months.</td>
<td>nasal and/or throat irritation (hot, peppery or burning sensation), rhinitis, tearing, sneezing, cough, headache</td>
<td>• Patient can titrate therapy to manage withdrawal symptoms</td>
<td>$3.40 (8 doses)</td>
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<tr>
<td><strong>Oral Inhaler</strong></td>
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<tr>
<td>Nicotrol Inhaler® 10mg cartridge delivers 4mg inhaled nicotine vapor in 80 puffs</td>
<td>6-16 cartridges/day; individualized dosing Decrease use over 6 months.</td>
<td>mouth and/or throat irritation, bad taste, cough, rhinitis, dyspepsia, hiccups, headache</td>
<td>• Mimics hand-to-mouth ritual of smoking  • Patient can titrate therapy to manage withdrawal symptoms</td>
<td>$5.82 (6 cartridges)</td>
</tr>
</tbody>
</table>

1 Nonprescription product distributed by GlaxoSmithKline  
2 Nonprescription product distributed by Watson Laboratories  
3 Nonprescription product distributed by Perrigo Company  
4 Nonprescription product distributed by Novartis Consumer Health  
5 Prescription product distributed by Schein Pharmaceuticals  
6 Nonprescription product distributed by Perrigo Company  
7 Prescription product distributed by Pharmacia  

Gum, although some patients may require extended use.

**Transdermal Nicotine Patch**

Transdermal nicotine systems consist of an impermeable backing layer, a drug-containing reservoir, an adhesive layer, and a removable protective liner. The amount of nicotine absorbed from the different formulations averages 68-98% of the labeled dose. Dosing schedules for the products vary (Table 2). Treatment for 8 or fewer weeks has been demonstrated to be as effective as longer treatment periods.9 There is no evidence that tapering the dose is more effective than abrupt withdrawal. Dosing is dependent on the number of cigarettes smoked per day. Other factors that should be considered include prior experience with the patch, degree of addiction, and whether the patient experiences strong cravings for cigarettes upon waking in the morning. In general, heavy smokers will require higher doses for a longer duration. For patients smoking 10 or fewer cigarettes a day, consider recommending a lower-strength patch.
The 16- and 24-hour patches have similar efficacy; however, patients with patch-related sleep disturbances (abnormal dreams, insomnia) may tolerate the 16-hour patch better, and patients with strong morning cravings may have more success with a 24-hour patch. Some patients may need to switch patch strengths during the first two weeks of therapy. Those experiencing substantial withdrawal symptoms or cigarette cravings should increase to a higher dose. Patients experiencing side effects (dizziness, perspiration, nausea, vomiting, diarrhea, headache, abdominal pain) should use the next lower dose. Skin reactions to the adhesive in the patch are common (up to 50%) and can be treated with 1% hydrocortisone cream. Because the adhesives vary among products, patients experiencing a skin reaction might consider switching brands.

**Nicotine Nasal Spray**
Nicotine nasal spray (Nicotrol® NS) is an aqueous solution of nicotine for administration to the nasal mucosa. Each actuation delivers a 50-microliter spray containing 0.5mg of nicotine. It is available in 10ml bottles; each bottle delivers approximately 200 applications. For best results, patients should be encouraged to use at least the recommended minimum of 8 doses per day. In the first week of use, patients will experience a hot, peppery feeling in back of the throat or nose, sneezing, coughing, watery eyes, or runny nose.

Nasal/airway reactions are common; 94% of patients report moderate to severe irritation in the first 2 days of therapy and 81% still report nasal irritation (mild to moderate) after 3 weeks. Because these side effects subside over time, patients should be advised not to stop using the medication. This product is not recommended for patients with known chronic nasal disorders (allergic rhinitis, polyps, sinusitis) or those with severe reactive airway disease, as bronchospasm has been reported in patients with asthma.

Of the currently FDA-approved NRT formulations, the nasal spray has the highest dependence potential, because its rapid onset of action (<10 minutes) most closely resembles cigarette smoking. The recommended duration of treatment is 3 to 6 months.

**Nicotine Inhaler**
The nicotine inhaler (Nicotrol® Inhaler) consists of a plastic mouthpiece and a plastic cartridge that delivers nicotine as an inhaled vapor from a porous plug containing 10mg of nicotine. Each cartridge releases 4 mg of nicotine during 80 inhalations, of which about 2 mg is absorbed. When puffed, the nicotine is vaporized and absorbed across the mouth and throat mucosa. The inhaler should be used longer and more often at first to help control cigarette cravings. Less nicotine per puff is released from the inhaler compared to a cigarette. The inhaler provides the smoker with adequate amounts of nicotine to reduce the urge to smoke, and may provide some degree of comfort by providing a hand-to-mouth ritual similar to smoking. Patients may initially experience mild local irritation (40%) of the mouth or throat, cough (32%), or rhinitis (23%); these adverse effects decrease with repeated use.

**Bupropion Sustained-Release (SR)**
In 1997, the FDA approved bupropion SR (Zyban®) as the first non-nicotine medication for smoking cessation. This agent, which was originally marketed as an antidepressant (Wellbutrin®), is thought to promote smoking cessation by blocking re-uptake of the neurotransmitters dopamine and norepinephrine, thus reducing cravings for nicotine and symptoms of withdrawal. Therapy is initiated with 150 mg every morning for three days, followed by 150 mg twice daily (at least 8 hours apart) for 7-12 weeks. Because steady-state levels are reached after about seven days, patients set their quit date for one to two weeks after starting therapy. For patients who are unable to stop smoking by week 7, therapy should be discontinued. Dose tapering is not necessary.

Bupropion is generally well tolerated. Common side effects include insomnia (30-40%) and dry mouth (11%); these usually lessen with continued use. Side effects that are less common but require discontinuation of treatment include tremors (3.4%) and rash (2.4%). Because seizures have been reported in approximately 1 out of every 1000 patients, bupropion is contraindicated in patients with a seizure disorder or a current or prior diagnosis of bulimia or anorexia nervosa. It should be administered with extreme caution to patients with a history of seizures or factors known to increase the risk of seizures, including CNS tumor and concurrent use of medications known to lower the seizure threshold. Bupropion SR is classified as pregnancy category B; it has not been studied in pregnant women. It can be used safely with NRT. Because bupropion is metabolized by the cytochrome P450 enzyme CYP2B6, drugs that induce the P450 enzymes (e.g., carbamazepine, phenytoin, phenobarbital) may increase the metabolism of bupropion, thereby decreasing its effects. Conversely, medications that inhibit P450 (e.g., cimetidine, ritonavir) may increase bupropion-related toxicity. By an unknown mechanism, the risk of acute bupropion toxicity is increased with concomitant administration of monoamine oxidase (MAO) inhibitors; the manufacturer recommends that MAO inhibitors be discontinued at least two weeks before initiation of bupropion. Disproportionately high incidences of adverse effects are seen in per-
sons taking levodopa (Parkinson’s disease); these patients should be started on lower doses and titrated upward with caution.

The advantages of bupropion include: (1) an oral formulation with twice-a-day dosing, (2) no risk of nicotine toxicity if the patient continues to smoke, (3) can be used with NRT, and (4) may be beneficial for use in patients with depression. Bupropion should not be used during pregnancy unless it is the only option and the patient is being monitored by a physician. Disadvantages include insomnia and a rare risk of seizures. Patients who experience insomnia should be advised to take their second dose in the afternoon, at least 8 hours after the first dose. The cost of therapy, based on the average wholesale price, is $3.21 per day. Bupropion approximately doubles quit rates compared to placebo.

**Selection of Pharmacologic Therapy**

Currently, there is little evidence that one medication for cessation is more effective than another. Selection of an agent should be individualized for each patient, taking into consideration patient preference, previous experience with quitting, whether the patient is able to obtain a prescription, medication compliance issues, and patient characteristics (e.g., medical concerns or contraindications, history of depression, concern about weight gain, level of smoking). Bupropion may be preferable to NRT in patients with a history of depression. Most research trials have evaluated the use of a single medication. More recently, however, investigators have reported improvements in quit rates when medications are used in combination. For example, there is evidence that use of the nicotine patch with either the nicotine gum or the nicotine nasal spray yields higher cessation rates.

Similarly, use of bupropion in combination with the nicotine patch has been shown to increase cessation rates 5.2 percentage points, from 30.3% to 35.5%, although the increase was not statistically significant. In general, combination therapy should be reserved for patients who have been unable to quit using a single agent.

**Conclusion**

As key contributors to patient care, it is important that pharmacists be active in identifying tobacco users and assisting patients with quitting. By applying the Five “A”s and combining drug therapy with the counseling techniques described above, the pharmacy profession could have a significant impact in reducing the public health burden of tobacco use in the United States.

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**Table 3. Counseling Tips**

**Before recommending a treatment plan, ask:**

- **What type and how much tobacco is used?**
  - This is needed to recommend a specific treatment dosage and to understand the patient’s level of addiction.

- **Review previous quit attempts—What worked, what didn’t? Why or why not?**
  - Assess the adequacy of dose and compliance with previous treatment regimens. Understand the patient’s beliefs about the various medications before offering suggestions. Discuss reasons for past relapses.

- **What are reasons and motivations for wanting to quit?**
  - Having a patient think about these issues raises his or her awareness about the importance of quitting.

- **How much confidence do you have in your ability to quit?**
  - A patient must believe that he or she is able to quit. If not, failure is imminent and the patient should be encouraged to try to quit at a later date, when he or she is ready.

- **What routines and triggers are associated with smoking?**
  - Understanding a patient’s routines and triggers will help to design coping strategies.

- **What are potential contraindications to smoking cessation medications?**
  - Determine whether a physician consult is needed.

**Before administering a treatment plan:**

- **Discuss the different methods / products for quitting.**
  - Present pros and cons of different methods, ruling out products that are contraindicated for the patient.

- **Help the patient set a quit date.**
  - This date should be more than 3 days but less than 14 days away, unless the patient has been prescribed bupropion, in which case the quit date should be 1-2 weeks after starting the medication.

- **Discuss coping strategies and request commitment to quit.**
  - Advise the patient to discard all cigarettes and to change their routine. Diversify tasks, avoid triggers for tobacco use, plan something enjoyable to do everyday, increase fluid intake, and reduce caffeine consumption. Advise the patient not to drink alcohol or socialize with other smokers during the early stages of quitting. The patient should enlist the support of family, friends, and coworkers. Discuss methods to reduce stress (relaxation, visualization, deep breathing). Review the patient’s commitment to quit, emphasizing the cons of continued smoking.

- **Discuss withdrawal symptoms and weight gain.**
  - Most symptoms begin in the first 24 hours after quitting, peak in 1-2 weeks and resolve within 30 days. Cravings may last longer. Advise patients to focus on quitting first, before worrying about weight gain. Encourage the patient to eat a healthy diet (as opposed to dieting) and increase physical activity if possible.

- **Counsel on appropriate use of medication(s) (if applicable).**
  - Review side effects, proper administration, and stress the importance of compliance with the treatment regimen.

- **Commend the patient for deciding to quit and offer to help throughout the quit attempt.**
  - Educate patient about the importance of receiving follow-up care.
Upon successful completion (70%) of the test, 1.5 hours of continuing pharmaceutical education credit (0.15 CEU'S) will be awarded in states that recognize ACPE approved providers. CE certificates are mailed every week for all successfully completed tests. Please allow 2-3 weeks after mailing your CE Credit Request for delivery of your certificate.

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**TEST QUESTIONS**

Write your answers on the Credit Request/answer form provided. To obtain additional Credit Requests, call toll free 800-798-3353. Photocopies are acceptable.

This program is valid through October, 2003.

Case history for questions 1-4.

FB, a 43-year old female, requests your assistance with stopping smoking. Upon questioning, you gain the following information:

Smoking 20 cigarettes per day for 25 years, history of moderate but controlled hypertension and bulimia; not pregnant, one previous failed quit attempt, cold turkey, one year ago. Current medications: 25mg atenolol once a day.

1. Which of the following medications would NOT be a reasonable choice for FB?
   a. bupropion  
   b. nicotine nasal spray  
   c. nicotine inhaler  
   d. nicotine gum

2. If FB chooses to use the nicotine patch and expresses strong early morning cravings to smoke, which would be most appropriate?
   a. Nicotrol® 15mg qd for 6 weeks
   b. Nicoderm CQ® 14mg qd for 6 weeks, followed by 7mg for 2 weeks
   c. Nicotine transdermal 11mg generic patch qd for 6 weeks
   d. Nicoderm CQ® 21mg qd for 6 weeks, followed by 14mg for 2 weeks and 7mg for 2 weeks

3. Which of the following patient education points would be CORRECT to provide FB?
   a. It is acceptable to continue smoking for the first 2 weeks of patch use.
   b. Use the same patch application site daily.
   c. Avoid wearing the patch while showering.
   d. Treat any mild redness of the skin at the patch site with 1% hydrocortisone cream.

4. If FB has difficulty sleeping while on a 24-hr patch, the MOST appropriate advice is to:
   a. Discontinue patch use.
   b. Remove the patch just before bedtime.
   c. Switch to a 16-hour patch.
   d. Take diphenhydramine 25mg before bedtime.

5. Each cartridge for the nicotine inhaler lasts for how many minutes of active puffing?
   a. 5 minutes  
   b. 20 minutes  
   c. 1-2 hours  
   d. 24 hours

6. Most nicotine withdrawal symptoms resolve within how many days of quitting?
   a. 1 day  
   b. 7 days  
   c. 30 days  
   d. 60 days

7. The recommended number of counseling sessions for helping patients to quit smoking is 4 to 8. Approximately what percentage of patients quit following 4-8 sessions?
   a. 21%  
   b. 31%  
   c. 50%  
   d. 75%

8. When counseling patients for tobacco cessation, which of the following are important issues to address?
   a. history of previous quit attempts
   b. reasons for wanting to quit
   c. routines associated with smoking
   d. all of the above

9. Most patients concerned about weight gain when quitting should be advised to:
   a. Follow a strict reduced calorie diet.
   b. Eat healthy foods during the quit attempt.
   c. Worry about quitting smoking first, then worry about losing weight.
   d. b and c

10. With which of the following products does nicotine most rapidly reach the brain?
    a. nicotine nasal spray  
    b. nicotine gum  
    c. nicotine patch  
    d. nicotine inhaler

11. In which of the following conditions should bupropion be avoided?
    a. anorexia or bulimia  
    b. hypertension  
    c. seizure disorder  
    d. a and c

12. Which of the following is CORRECT to tell patients starting bupropion therapy?
    a. Take 2 tablets daily for three days, then reduce to one tablet daily.
    b. Stop smoking BEFORE starting bupropion.
    c. If you experience difficulty sleeping, take your 2nd dose 8 hours after the first dose.
    d. If cravings continue, increase to 2 tablets bid.

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**The Risk of Venous Thrombosis with Newer Birth Control Pills**


**Summary:** Controversy exists as to whether oral contraceptives (COCs) containing third generation progestins (desogestrel, gestodene) are more likely to cause venous thrombosis than COCs containing other progestins (eg, levonorgestrel, norethindrone). This meta-analysis of data from 13 studies found that the risk of venous thrombosis was 1.7 times greater with third generation COCs compared to other COCs.

**Comment:** This new study lends credibility to the assertion that users of COCs with desogestrel or gestodene are at increased risk for venous thrombosis compared to users of other COCs. Prior to this meta-analysis, we reported in the September issue of *The Rx Consultant* that the risk was not significantly increased for users of third generation progestins. Clearly, the issue is not yet settled. Venous thrombosis occurs yearly in 10-15/100,000 COC users and 25/100,000 users of desogestrel/gestodene COCs. While there is an increase in risk, the number of women affected is small and the risk is higher during pregnancy (60/100,000 women) than with any COC. Death from venous thrombosis is uncommon (about 3%).

By Leslie A. Shimp, PharmD, MS

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**FDA Likely to Approve First IL-1Ra Agent, Anakinra (Kineret®, Amgen)**


**Summary:** Anakinra (Kineret®) is an interleukin-1 receptor antagonist (IL-1Ra) used to treat rheumatoid arthritis, either as monotherapy or in combination with other agents. Interleukin-1, like tumor necrosis factor, is a cytokine found in joint synovial fluid that is responsible for the destructive action in rheumatoid arthritis. Anakinra improves radiographic and clinical status, stops joint destruction, improves health-related quality of life, and restores functional ability in patients with active rheumatoid arthritis. The drug is self-administered as a single 1ml subcutaneous injection at 30, 75 or 150 mg/d.

**Comment:** Patients should be instructed to give the injection similar to an insulin injection, being sure to rotate sites on the abdomen, thighs, and backs of the upper arms. Some adverse effects seen with anakinra are mild and transient injection site reactions that usually resolve within 2-3 weeks, and less frequently, neutropenia and mild infections.

By: Rene L. Roberts, PharmD and Ralph E. Small, PharmD

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**New Guidelines on Anti-retroviral Therapy and Post-exposure Prophylaxis (PEP)**

http://www.hivatis.org

**Summary:** New treatment guidelines have recently been published on anti-retroviral therapy in pediatric patients, adults, and pregnant women. New guidelines are also available on the management of opportunistic infections, and for post-exposure prophylaxis in health care workers after occupational exposures to HIV, hepatitis B, and hepatitis C. Post-exposure antiretroviral options have been expanded to include stavudine (Zerit®) and didanosine (Videx®). Previously, only zidovudine (Retrovir®) and lamivudine (Epivir®) were recommended. Additional agents such as protease inhibitors can be added for higher risk exposures. More aggressive antiretroviral combinations are also recommended in pregnancy. Updated information about the teratogenicity of these agents is included.

**Comment:** These reviews should be key resources in any pharmacy that prides itself on providing state-of-the-art HIV drug information to patients and health care providers.

By: Betty J. Dong, PharmD
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