First-Line Treatments for Smoking Cessation


Target Audience
This activity was developed specifically for pharmacists and pharmacy technicians.

Pharmacist Learning Objectives
At the end of this activity, participants should be able to:
1. List the first-line treatments for smoking cessation, categorized by over-the-counter vs. prescription availability and nicotine replacement therapy vs. non-nicotine replacement therapy.
2. Outline a treatment plan for specific patients based on concomitant medical conditions/medications, previous attempts to quit, willingness to quit, access to a prescriber, adherence and other measures.
3. Explain the mechanism of action for both bupropion SR and varenicline and how they are different from nicotine replacement therapy.

Pharmacy Technician Learning Objectives
At the end of this activity, participants should be able to:
1. List the first-line treatments for smoking cessation, categorized by over-the-counter vs. prescription availability and nicotine replacement therapy vs. non-nicotine replacement therapy.
2. Explain how to compare and contrast the manufacturer suggested treatment schedules for the available smoking cessation treatments.
3. Memorize the steps for quitting smoking as outlined by the Centers for Disease Control and Prevention.

Disclosure Statement
The author has indicated that he does not have any conflicts of interest, nor does he have financial relationships with a commercial interest related to this activity.

Introduction

Data from the World Health Organization (WHO) suggests that over 1.1 billion people worldwide smoked tobacco in 2015. The Centers for Disease Control and Prevention (CDC) report that 15.1 percent of adults over 18 in the United States (U.S.) were cigarette smokers in 2015. This equates to 36.5 million adults smoking in the U.S., 68 percent of whom reported that they wanted to stop smoking completely. Fifty-five percent of the total smokers in 2015 reported an attempt at quitting in the past year while only 7.4 percent were able to achieve smoking cessation. This suggests an opportunity for pharmacists to make an impact on patients and provide support in their smoking cessation efforts. Pharmacists can assist patients by counseling on the importance of quitting, motivating those who already want to try quitting or supporting those who are amidst an effort to quit.
Health Consequences

Smoking is a major contributor to morbidity and mortality and places a significant financial burden on smokers, their families and the healthcare system. The Surgeon General reported in 2014 that cigarette smoking is responsible for more than 480,000 American deaths each year.³ This is more than the human immunodeficiency virus (HIV), illegal drug use, alcohol abuse, motor vehicle injuries and firearm incidents combined.⁴ Among the list of health consequences from smoking are cancer, heart disease, stroke, rheumatoid arthritis and chronic obstructive pulmonary disease (COPD).⁵ Smoking is reportedly the cause of nine out of 10 deaths from lung cancer and eight out of 10 deaths from COPD.³ The Surgeon General’s report also gives information on increased risk for morbidities from smoking. Coronary heart disease and stroke both increase by a factor of two to four, while developing lung cancer increases by over 25 times.³

Financial Burden

A smoker with a pack-per-day habit can spend roughly $2,200 each year on cigarettes. Patients must be educated on how the detrimental health effects of smoking can increase this financial burden exponentially. For some perspective, a 2010 study showed that from 2006 to 2010 the annual healthcare spending attributed to cigarette smoking in the United States was $170 billion.⁶ This is a combination of dollars spent on inpatient, non-inpatient and through prescription drugs. Of this $170 billion, it is estimated that over 60 percent comes from Medicare, Medicaid and other federally funded programs.⁶

Pharmacists’ Role

Pharmacists are in a unique position to provide a high level of care and support as patients quit smoking. Pharmacists are often considered the most accessible healthcare professionals.⁷ While it takes time to see physicians, nurses, physician assistants and nurse practitioners outside of the emergency room, pharmacists are typically available to counsel during business hours and even 24 hours-a-day in some locations. It is no surprise that pharmacist-led smoking cessation programs in community pharmacies have become very successful. To demonstrate this, a large study was done in 2014 which combined data from five trials with a control arm receiving standard usual care and the intervention arm receiving pharmacy services. The intervention group increased clinically validated abstinence with relative risk (RR) of 3.21 (95 percent CI, 1.81-5.72) compared to control. This means that patients experiencing pharmacy interventions were 3.21 times more likely to achieve smoking abstinence. Additionally, the RR for short-term abstinence was 2.48 (95 percent CI, 1.15-5.31) and for long-term abstinence was 2.4 (95 percent CI, 1.37-4.23).⁸ The data being compiled to support the utility of pharmacists in smoking cessation interventions has put an increased demand on the profession to enhance their expertise in this area. The remainder of this article will provide a working knowledge of the suggested treatments for smoking cessation.

Treatments

Nicotine Replacement Therapy (NRT)
The U.S. Department of Health and Human Services (DHHS) considers five forms of nicotine replacement therapy (NRT) and two forms of non-nicotine replacement therapy (NNRT) as first-line treatments to aid in smoking cessation. The five forms of NRT include nicotine gum, inhaler, lozenge, nasal spray and patches. Of these, the gum, lozenges and patches are available as over the counter (OTC) products without a prescription. For this reason NRT is often the first pharmacologic method patients use to help them quit smoking. Smoking cessation is aided by NRT because it reduces physiological or psychomotor withdrawal symptoms, two common reasons why abstinence fails. Studies have determined that using these NRT strategies can double the likelihood of quitting. The mechanism of action for these medications is twofold with the primary action being stimulation of the same receptors that are affected by nicotine in cigarettes. Nicotinic receptors in the brain induce dopamine release, which reduces withdrawal symptoms. NRT is unable to fully eliminate withdrawal symptoms likely for the following reason. Inhalating a cigarette gives a rapid and large increase in arterial nicotine that reaches the brain in seconds to produce euphoric effects. Because NRTs rely on venous absorption, the delay in effect can vary from minutes to hours and produce little to no euphoric effect.

Nicotine gum was introduced in the U.S. as a prescription-only product in the 1980’s and has since become an OTC product offered in both 2 mg and 4 mg pieces. The following warnings and directions are included in the packaging for Nicorette Gum.

- **Directions:**
  - If you are under 18 years of age, ask a doctor before use.
  - Stop smoking completely when you begin using the gum.
  - **Dosage:**
    - If you smoke your first cigarette within 30 minutes of waking up, use 4 mg nicotine gum.
    - If you smoke your first cigarette more than 30 minutes after waking up, use 2 mg nicotine gum.
  - **How much and how to take:**
    - 1 piece every 1-2 hours in weeks 1-6, 1 piece every 2-4 hours weeks 7-9, and 1 piece every 4-8 hours weeks 10-12
    - Chew slowly until it tingles. Then park it between your cheek and gum. When the tingle is gone, begin chewing again, until the tingle returns.
      - Repeat this process until most of the tingle is gone (about 30 minutes).
  - Do not eat or drink for 15 minutes before chewing or while chewing.
  - To improve your chances of quitting, use at least 9 pieces per day for the first 6 weeks.
  - If you experience strong or frequent cravings, you may use a second piece within the hour. However, do not continuously use one piece after another since this may cause hiccups, heartburn, nausea or other side effects.
  - Do not use more than 24 pieces a day.
- It is important to complete treatment. Stop using the nicotine gum at the end of 12 weeks. If you still feel the need to use nicotine gum, talk to your doctor.

- **Warnings:**
  - If you are pregnant or breast-feeding, only use this medicine on the advice of your healthcare provider.
  - Do not use if you continue to smoke, chew tobacco, use snuff, apply a nicotine patch or use other nicotine containing products.
  - Stop use and ask a doctor if:
    - Mouth, teeth, or jaw problems occur.
    - Irregular heartbeat or palpitations occur.
    - You get symptoms of nicotine overdose such as nausea, vomiting, dizziness, diarrhea, weakness, and rapid heartbeat.
    - Oral blistering occurs.
    - You have symptoms of an allergic reaction (such as difficulty breathing or rash).

Nicotine lozenges are another OTC option for NRT and are supplied in both 2 mg and 4 mg sizes. This dosage form is similar to the gum in many ways and carries the same warnings and precaution. The schedule for use is the same as recommended for nicotine gum. During weeks 1-6 use one piece every 1-2 hours. During weeks 7-9 use one piece every 2-4 hours. During weeks 10-12 use one piece every 4-8 hours, at which time treatment should be discontinued. Notable differences in directions for use include the following:

- Place the lozenge in your mouth and allow the lozenge to slowly dissolve. Minimize swallowing. Do not chew or swallow lozenge.

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**STOP AND REFLECT**

A patient presents to your pharmacy requesting a suggestion for which nicotine gum product they should purchase. She is a 17-year-old female who reports a pack-per-day smoking habit and begins each day by immediately smoking a cigarette. The patient reports the reason for her quitting attempt today is that she believes she may be pregnant. How will the information provided by your patient influence your treatment suggestions?

**Feedback:** The two biggest concerns for this patient are her age and possible pregnancy. Patients who are pregnant and/or under 18 years of age should consult with their doctor before starting on any NRT. Additionally, the patient has not said if she is currently smoking. It is important that patients are not using cigarettes, chewing tobacco, snuff, nicotine patches, or any other nicotine containing products while using nicotine gum. Because the patient has her first cigarette less than 30 minutes after waking up, we should suggest using the 4 mg pieces (if she were eligible to start NRT).
• Do not use more than five lozenges in six hours. Do not use more than 20 lozenges per day.
• You may feel a warm or tingling sensation
• Occasionally move the lozenge from one side of your mouth to the other until completely dissolved
• Do not use more than one lozenge at a time or continuously use one lozenge after another since this may cause you hiccups, heartburn, nausea, or other side effects

The last NRT available OTC in the U.S. to be discussed are the nicotine patches. The product is designed to be used as one patch per day applied for 24 hours. Based on the number of cigarettes a patient smokes per day, transdermal nicotine patches should be tapered on a preset schedule. Various patch strengths exist; however, the most commonly used patches deliver 7 mg, 14 mg or 21 mg of nicotine per 24 hours. Notable differences between these patches and the gum/lozenges listed above include the following:

• Do not smoke even when not wearing the patch. The nicotine in your skin will still be entering your bloodstream for several hours after you take off the patch
• If you have vivid dreams or other sleep disturbances remove the nicotine at bedtime
• Used patches have enough nicotine to poison children and pets. If accidentally swallowed, get medical help or contact a Poison Control Center immediately. Save the pouch to use for patch disposal. Dispose of the used patches by folding sticky ends together and putting in the pouch. Be sure to keep the pouch out of reach of children and pets.
• Schedule for use:
  - If you smoke more than 10 cigarettes per day
    • Step 1: Use one 21 mg patch/day in weeks 1 through 4
    • Step 2: Use one 14 mg patch/day in weeks 5 through 6
    • Step 3: Use one 7 mg patch/day in weeks 7 and 8 then stop
  - If you smoke 10 or less cigarettes per day
    • Step 1: Use one 14 mg patch/day in weeks 1 through 6
    • Step 2: Use one 7 mg patch/day in weeks 7 and 8 then stop
• Directions for use:
  - Apply one new patch every 24 hours on skin that is dry, clean, and hairless.
  - Remove backing from patch and immediately press onto skin. Hold for 10 seconds.
  - Wash hands after applying or removing patch. Save the pouch to use for patch disposal. Dispose of the used patches by folding sticky ends together and putting in pouch.
  - The used patch should be removed and a new one applied to a different skin site at the same time each day.
  - If you have vivid dreams, you may remove the patch at bedtime and apply a new one in the morning.
  - Do not wear more than one patch at a time.
  - Do not cut patches in half or into smaller pieces.
Do not leave patch on for more than 24 hours because it may irritate your skin and loses strength after 24 hours.

To avoid possible burns, remove patch before undergoing any MRI procedures.

Stop using the patch at the end of eight weeks. If you still feel the need to use the patch talk to your doctor.

For patients who fail the above OTC products or would prefer not to use these dosage forms, nicotine for smoking cessation is also available as an inhaler and nasal spray. The branded Nicotrol inhaler is the only nicotine inhaler currently available in the U.S. and requires a prescription from a doctor. With this delivery method, nicotine is absorbed in the mouth and throat before reaching the bloodstream. Each cartridge contains 10 mg of nicotine with 4 mg delivered. As with other nicotine products there is a tapering schedule with the nicotine inhaler, which should be completed by the end of six months. Package insert information unique to the inhaler includes the following:

- Your doctor may adjust the number of inhaler cartridges during the first few weeks. As your body adjusts to not smoking, your doctor will either tell you to stop using the inhaler or slowly reduce the dose.
- Patients are more successful in quitting smoking if they combine the inhaler with support groups, counseling or specific behavioral change techniques.
- Side effects: many people experience mild irritation of the mouth or throat and cough when they first use the Nicotrol Inhaler. Most people get used to these effects in a short time. Stomach upset may also occur.
- Keep out of reach of children and pets, even small amounts can cause serious illness. If a child chews or swallows Nicotrol Inhaler cartridges, call a doctor or Poison Control Center. After a cartridge is used, throw it away out of reach of children and pets. Even used cartridges contain enough nicotine to seriously harm children and pets. The Nicotrol Inhaler is a child resistant product. Please read carefully the instructions regarding how to open, close and lock.
- Tell your doctor if you have overactive thyroid, diabetes requiring insulin, kidney or liver disease, stomach ulcers or wheezing/asthma. This is in addition to the list provided under nicotine gum which applies to all NRT.
- Directions for use:
  1. Follow doctor’s directions. Stop smoking completely during the Nicotrol Inhaler treatment program.
  2. Remove mouthpiece from plastic wrap. Push the top and bottom together and turn the two pieces to line up the markings. Pull the top and bottom apart.
  3. Take out cartridge tray. Peel back to release one cartridge and insert cartridge into Inhaler. Push hard on the cartridge until it pops down into place.
4. Line up the markings again and push the two pieces back together so they fit tight. Turn the top and bottom pieces so the markings do not line up and it is locked again. Store cartridges in plastic case when not in use.

5. Inhale deeply into back of throat or puff in short breaths. As you inhale or puff through the mouthpiece, nicotine turns into a vapor and is absorbed into your mouth and throat. Use the Inhaler longer and more often at first to help control cigarette cravings.

6. Nicotine in cartridges is used up after about 20 minutes of active puffing. Try different schedules to help control cravings. Puffing on the Inhaler for five minutes at a time will give you enough nicotine for four uses. In a few days you’ll find what works best and know when nicotine in cartridges is used up. Use the Inhaler at room temperature (above 60°F). Cold temperatures reduce the amount of nicotine you inhale.

7. When the cartridge is empty, take off top of mouthpiece. Throw the used cartridge away, out of reach of children and pets. When not in use keep the mouthpiece in the locked position and always store mouthpiece and cartridges in plastic case, out of reach of children and pets.

- Do not use more than 16 cartridges each day unless directed to do so by your doctor.
- Do not use longer than six months.
- Store at room temperature, not to exceed 77°F (25°C).
- If you keep cartridges in a car, be careful as interiors heat up quickly
- Protect from light.
- Clean mouthpiece regularly with soap and water.

The final NRT available in the U.S. is the nicotine nasal spray and must be purchased from a pharmacy with a valid prescription from a doctor. The product is only available as the brand name Nicotrol NS and comes in a 10 mg/mL strength. Initiation of this medication is similar to the inhaler in that doctors can increase or decrease dosage in the first few weeks based on patient reaction. Highlighted below are some of the differences between the nicotine inhaler the nasal spray.17

- Side effects:
  - During the first week or so most people experience the following side effects: hot, peppery feeling in back of throat or nose, sneezing, coughing, watery eyes or runny nose. Wait five minutes before driving.
  - Be sure to use regularly for the first week to help adjust to side effects.

- Keep out of reach of children and pets as Nicotrol NS can cause serious illness even in very small amounts. If a child uses or handles Nicotrol NS, call a doctor or Poison Control Center. When the bottle is empty, replace cap and throw it away out of reach of children and pets. Even empty bottles contain enough nicotine to seriously harm children and pets.
Tell your doctor if you have chronic nasal problems such as nasal allergies, inflammation, sinusitis or nasal polyps

Read information on both sides before use.

- Take as directed by doctor, but not more than five times per hour or 40 times in 24 hours. Side effects will lessen for most people in a few days. If side effects do not lessen after a week, call your doctor.

Directions for use:

- Remove cap by pressing in circles on the sides of bottle and pull off cap.
- Prime pump (before first use). Get a tissue or paper towel and press up on the bottom with thumb to pump into tissue until you see a fine spray six to eight times. Throw tissue away.
- Blow nose if it is not clear. Tilt head back slightly.
- Insert tip of bottle into nostril as far as is comfortable. Breathe through mouth. Spray once in each nostril. Do not sniff or inhale while spraying. If nose runs, gently sniff to keep the Nasal Spray in nose. Wait two or three minutes before blowing nose.
- Place cap back on the bottle after use. Store at room temperature (below 86°F) out of reach of children. If you don’t use the Nasal Spray for 24 hours, prime pump in tissue one or two times. Most vials of Nicotrol NS contain 100 doses (200 sprays), but excessive priming will reduce the amount of medicine available for use. Avoid excessive priming.
- Avoid contact with skin, eyes and mouth. If bottle breaks, wear rubber gloves, wipe up with paper towel and wash surfaces thoroughly. Do not let nicotine come in contact with your skin, mouth or eyes. If it does, rinse with plain water immediately. Nicotine overdose can occur when nicotine is absorbed through the skin.
Non-Nicotine Replacement

Two other pharmacologic treatments for smoking cessation are suggested first-line by DHHS and include varenicline and bupropion. In 1997 bupropion became the first non-nicotine drug to be approved for aiding smoking cessation. Bupropion was first brought to market as an antidepressant that achieves its action in part through inhibition of both norepinephrine and dopamine reuptake pumps in the brain. The precise mechanism for bupropion in smoking cessation is not known, but is most often attributed to its effect on dopamine reuptake.

Nicotine has shown to have both a direct and indirect stimulatory effect on dopamine release within the mesolimbic area of the brain. Indirect dopamine secretion is achieved when nicotine activates glutamatergic and gamma aminobutyric acid (GABAergic) neurons within the ventral tegmental area (VTA) of the brain. Glutamate is a stimulating neurotransmitter, and when released from glutamatergic neurons, will stimulate dopamine release from nearby dopaminergic neurons. GABA suppresses secretions from dopaminergic neurons because it is an inhibitory neurotransmitter. Desensitization of the nAChRs on both the glutamatergic and GABAergic neurons dictates the amount of dopamine secreted. Studies have shown that nAChRs on the GABA neurons desensitize faster and at a lower nicotine concentration than those on glutamatergic neurons. This gives a net balance of dopaminergic neuron excitation and dopamine secretion. Nicotine can also directly increase dopamine release by stimulating nAChRs on dopaminergic neurons within the VTA. Dopaminergic neurons release dopamine into the nucleus accumbens (NAc), a site known for controlling reward, reinforcement and pleasure. Bupropion plays an important role by blocking dopamine reuptake. When a patient quits smoking, nicotine is no longer there to increase dopamine levels, and bupropion can help by preventing synaptic dopamine reuptake. This increases the effects of the dopamine that is released in lower concentrations than during smoking.

Bupropion was originally developed as an antidepressant medication and began trials as a smoking cessation aid much later due to reports that patients taking bupropion for depression were more likely to quit smoking while on the medication. A 1997 double-blind, placebo controlled, randomized controlled trial demonstrate the superiority of bupropion SR to placebo at both seven weeks and 12 months from initiation. At seven weeks, the rate of smoking cessation was 19 percent, 28.8 percent, 38.6 percent and 44.2 percent in the placebo, 100 mg/d, 150 mg/d and 300 mg/d groups, respectively. At 12-months, the rate of smoking cessation was 12.4 percent, 19.6 percent, 22.9 percent and 23.1 percent for each group, respectively.

The following comes directly from the package insert for Zyban (bupropion) and includes pertinent information to be passed on to patients:

- Dosage and Administration:
  - Starting dose: 150 mg per day for first three days.
  - General: increase dose gradually to reduce seizure risk.
  - Begin dosing one week before quit day.
o After three days, increase the dose to 300 mg per day, given as 150 mg twice daily at an interval of at least eight hours.

o May be used with nicotine transdermal system.

o Moderate to severe hepatic impairment: 150 mg every other day.

o Mild hepatic impairment: consider reducing the dose and/or frequency of dosing.

o Renal impairment: consider reducing the dose and/or frequency.

- Quitting Smoking:
  o Symptoms of nicotine withdrawal: urge to smoke, depressed mood, trouble sleeping, irritability, frustration, anger, feeling anxious, difficulty concentrating, restlessness, decreased heart rate, increased appetite and weight gain.

  o Stop taking Zyban and call your healthcare provider right away if you, your family or caregiver notice any of the following symptoms: changes in behavior or thinking, aggression, hostility, agitation, depression, suicidal thoughts or actions.
    - Tell your healthcare provider before starting Zyban if you have ever had depression or other mental health problems.

- Depression/Serious Mental Conditions and Suicidal Thoughts or Actions
  o Antidepressant medications may increase suicidal thoughts or actions in some children, teenagers or young adults within the first few months of treatment.

  o People who have (or have a family history of) bipolar illness (also called manic-depressive illness) or suicidal thoughts or actions and at a higher risk of suicidal thoughts or actions.

  o Pay close attention to changes, especially sudden changes, in mood, behaviors, thoughts or feelings. This is very important when an antidepressant medicine is started or when the dose is changed.

  o Keep all follow-up visits with your healthcare provider as scheduled.

  o Call your healthcare provider if you or your family member has any of the following symptoms, especially if they are new, worse or worry you:
    - Thoughts about suicide or dying
    - Attempts to commit suicide
    - New or worse depression
    - New or worse anxiety
    - Feeling very agitated or restless
    - Panic attacks
    - Trouble sleeping (insomnia)
    - New or worse irritability
    - Acting aggressive, being angry or violent
    - Acting on dangerous impulses
    - An extreme increase in activity and talking (mania)
    - Other unusual changes in behavior or mood

  o Never stop taking Zyban without first talking to a healthcare provider.

  o Some people get high blood pressure that can be severe, while taking Zyban.
- Chances may be higher if using NRT to help you stop smoking.
- Visual problems such as eye pain, changes in vision or swelling or redness in or around the eye.
- Do not take Zyban if you:
  - Have or had seizure disorder or epilepsy.
  - Have or had an eating disorder such as anorexia nervosa or bulimia.
  - Are taking any other medicines that contain bupropion, including Wellbutrin, Wellbutrin SR, Wellbutrin XL, Aplenzin or Forfivo XL.
  - Drink a lot of alcohol and abruptly stop drinking, or take medicines called sedatives (these make you sleepy), benzodiazepines, or anti-seizure medicines, and you stop taking them all of a sudden.
  - Take a monoamine oxidase inhibitor (MAOI). Ask your healthcare provider or pharmacist if you are not sure if you take and MAOI, including the antibiotic linezolid.
    - Do not take an MAOI within two weeks of stopping Zyban unless directed to do so by your healthcare provider.
    - Do not start Zyban if you stopped taking an MAOI in the last two weeks unless directed to do so by your healthcare provider.
- Tell your healthcare provider about your other medical conditions, including if you:
  - Have liver problems, especially cirrhosis of the liver.
  - Have kidney problems.
  - Have, or have had, an eating disorder such as anorexia nervosa or bulimia.
  - Have had a head injury.
  - Have had a seizure (convulsion, fit).
  - Have had a tumor in your nervous system (brain or spine).
  - Have had a heart attack, heart problems or high blood pressure.
  - Are a diabetic taking insulin or other medicines to control your blood sugar.
  - Drink alcohol.
  - Abuse prescription medicines or street drugs.
  - Are pregnant or plan to become pregnant.
- Are breastfeeding. Zyban passes into your milk in small amounts.

The newest first-line treatment for smoking cessation is varenicline (Chantix). A novel two-part mechanism of action was suggested for this medication in a 2005 study that analyzed the effects of varenicline as a partial agonist of the nAChR α4β2.\textsuperscript{28} As discussed above, agonist activity from nicotine on nAChRs promotes release of dopamine and its pleasurable and rewarding effects. As a partial agonist of α4β2 varenicline can provide patients with some of the dopamine release that is absent due to lack of nicotine. The other proposed mechanism involves the competitive nature in which varenicline binds to α4β2, not allowing nicotine to agonize the receptors and induce dopamine release. Without the release of dopamine, relapse becomes less likely due to the loss of pleasure felt by smoking.

A 2008 pooled analysis study of two trials demonstrated the superiority of varenicline to both bupropion SR and placebo in smoking cessation rates at intervals of nine to 12 months.\textsuperscript{29,30,31} Both trials were set up in the same way, comparing smoking cessation rates between patients taking varenicline 1 mg twice daily, bupropion SR 150 mg twice daily and placebo. Both were double-blind, double-dummy, placebo-controlled, randomized multicenter trials following patients for a treatment length of 12-weeks with a follow-up length of 40 nontreatment days. The pooled results after the 40 day follow-up for smoking cessation showed varenicline at 44 percent, bupropion at 29.7 percent and placebo at 17.7 percent.\textsuperscript{29} This demonstrates a statistically significant benefit to treating with varenicline 1 mg twice daily over bupropion SR 150 mg twice daily for smoking cessation.

Stop and Reflect
A 40-year-old female patient presents to your pharmacy to pick up a refilled prescription for her father for Zyban which has been helping him quit smoking. She asks for a minute of your time in the consultation room to discuss if she might be a candidate to use Zyban to help her quit smoking as well. Her past medical history included mild alcoholic cirrhosis, childhood seizures, GERD and depression for which she is currently only taking omeprazole and selegiline. What concerns do you have for her before you would suggest she ask her doctor to prescribe Zyban?

Feedback: From her past medical history the cirrhosis and seizure history should be addressed. Cirrhosis suggests decrease liver function and her doctor would likely consider starting Zyban at a lowered dose if at all. Zyban can increase risk for seizures and should be used with caution in patients with a history of seizures. She is untreated for seizures and has not had one in years, but her doctor should discuss the risks with her. You should talk about her current alcohol intake and warn against suddenly stopping drinking while taking Zyban.

Finally, selegiline is an MAOI and should not be taken in conjunction with Zyban. It is suggested that you do not start Zyban until it has been at least two weeks since you last took an MAOI unless directed to do so by your healthcare provider.
The following information comes from the package insert for Chantix (varenicline):

- Stop taking Chantix and call your healthcare provider right away if you, your family or caregiver notice new or worse mental health problems such as changes in behavior or thinking, aggression, hostility, agitation, depressed mood or suicidal thoughts or actions.
- Before taking Chantix, tell your healthcare provider if you have ever had depression or other mental health problems.
- Before taking Chantix, tell your healthcare provider if you:
  - Use other treatments to quit smoking. Using Chantix with a nicotine patch may cause nausea, vomiting, headache, dizziness, upset stomach and tiredness to happen more often than if you just use a nicotine patch alone.
  - Have kidney problems or get kidney dialysis. Your healthcare provider may prescribe a lower dose of Chantix for you.
  - Have a history of seizures.
  - Drink alcohol.
  - Have heart or blood vessel problems.
  - Have any other medical conditions.
  - Are pregnant or plan to become pregnant. It is not known if Chantix will harm your unborn baby.
  - Are breastfeeding. It is not known if Chantix passes into breast milk. If you breastfeed and take Chantix, monitor your baby for seizures as well as spitting up or vomiting more than normal.
- How to start taking Chantix: there are three different ways, talk to your healthcare provider before starting.
  1. Choose a quit date when you will stop smoking. Start Chantix one week (seven days) before your quit date. Take Chantix for 12 weeks.
  2. Start taking Chantix before you choose a quit date. Pick a date to quit smoking that is between eight and 35 days of treatment. Take Chantix for 12 weeks.
  3. If you are sure that you are not able or willing to quit smoking right away, start taking Chantix and reduce smoking during the first 12 weeks of treatment, as follows:
     a. Weeks one through four: reduce your smoking to reach one-half of your starting daily number of cigarettes.
     b. Weeks five through eight: reduce your smoking to reach one-quarter of your starting daily number of cigarettes.
     c. Weeks nine through 12: keep reducing your smoking until you are no longer smoking.
- Aim to quit by the end of the twelfth week of treatment, or sooner if you feel ready.
- Continue taking Chantix for another 12 weeks, for a total of 24 weeks.
- Chantix dosage:
  - Day one to day three: take 0.5 mg each day.
o Day four to day seven: take 0.5 mg in the morning and 0.5 mg in the evening.
o Day eight to end of treatment: take 1 mg in the morning and 1 mg in the evening.

- Take Chantix after eating and with a full glass (8 ounces) of water.
- Talk to your healthcare provider if you are having side effects such as nausea, strange dreams or sleep problems. Your healthcare provider may want to reduce your dose.
- Decrease the amount of alcoholic beverages that you drink during treatment with Chantix until you know if Chantix affects your ability to tolerate alcohol. Some people have experienced the following when drinking alcohol during treatment with Chantix:
  o Increased drunkenness (intoxication)
  o Unusual or sometimes aggressive behavior
  o No memory of things that have happened
- The most common side effects of Chantix include:
  o Nausea, constipation, gas, vomiting
  o Sleep problems (trouble sleeping or vivid, unusual or strange dreams)

**Behavioral Support**

Different modes of behavioral support have been added to pharmacotherapy to aid in smoking cessation, including documents containing advice on how to quit, group therapy sessions, individual counseling sessions, telephone or text message contacts and more. A 2009 study showed that a group receiving only cognitive behavioral group therapy (CBGT) had a 22.2 percent chance of being abstinent from smoking at the 19-week endpoint. This study paired standard bupropion SR dosing with CBGT, nonspecific psychological support in groups (NSGS), and brief counseling which showed odds of quitting at 19 weeks of 50.0 percent, 62.9 percent and 53.2 percent, respectively. A 2004 study investigating the rates of smoking cessation reported 12 week and 24 week quitting percentages of 57 and 40, respectively. In combination with the data above, this shows that bupropion SR combined with behavioral support produces higher cessation rates than either method alone. Many other studies have demonstrated that combinations of NRT or varenicline with behavioral support produce better results than any single intervention.

In addition to having knowledge concerning smoking cessation pharmacologic interventions, it is important that pharmacy professionals be able to counsel patients on how to build a plan for quitting. The CDC has published steps that can be taken to prepare patients for quitting and making them more successful. The following list summarizes the CDC recommended steps:

1. Pick a quit date: choose a date in the near future (usually within the next two weeks) that is not too busy or stressful.
   a. Make reminders for yourself until quit day to help you prepare.
2. Let loved ones know you are quitting.
   a. Let them know in advance of your quit day and lay out how they can be helpful.
3. Remove reminders of smoking including cigarettes, matches, ashtrays and lighters.
a. Cleaning your home and office can also help as the smell of cigarettes is often a cause of cigarette craving.
b. Don’t save a pack of cigarettes for emergency situations, it is better to throw away all cigarettes and matches. Give or throw away lighters and ashtrays.

4. Identify your reasons to quit smoking and remind yourself of them daily to inspire you to stop smoking for good.
5. Identify your smoking triggers.
   a. Certain activities, feelings and people are linked to your smoking. When you come across these things, they may “trigger” or turn on your urge to smoke.
6. Develop coping strategies for your nicotine withdrawal symptoms.

Conclusion

Statistics provided in this article demonstrate that educating patients on their options for smoking cessation aids is important and effective in helping patients quit. In addition, the statistics provide perspective on the number of lives and healthcare dollars that could be saved if smoking prevalence was decreased.

Patients working to quit have several options for pharmacologic treatment. These options include over-the-counter NRT such as nicotine gum, lozenges and patches as well as prescription NRT such as nicotine inhalers and nasal sprays. Other prescription medications for smoking cessation include bupropion and varenicline. Each of these interventions has unique instructions for use and come with risks and side effects. Pharmacists can play a role in smoking cessation by educating patients on how to use each medication and what can be expected throughout the course of treatment. Pharmacists are considered the most accessible healthcare providers and for this reason have a unique ability to closely follow and support patients in their attempts to quit smoking. By following up with patients over the phone and in pharmacies and clinics, pharmacist can act as a motivating force as well as answer questions that patients may have. In addition to these actions, it is important that pharmacists convey the efficacy of behavioral support in combination with pharmacologic treatment. Many studies have shown that combination treatment produces better smoking cessation results than either method alone. Patients can increase likelihood of long-term smoking abstinence by following the steps published by the CDC along with pharmacologic treatment and behavioral support.

References


