AIDS for CESSATION

METHODS for QUITTING

- Nonpharmacologic
  - Counseling and other non-drug approaches
- Pharmacologic
  - FDA-approved medications

Counseling and medications are both effective, but the combination of counseling and medication is more effective than either alone.

Fiore et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline.* Rockville, MD: USDHHS, PHS, May 2008.

NONPHARMACOLOGIC METHODS

- Cold turkey: Just do it!
- Unassisted tapering (fading)
  - Reduced frequency of use
  - Lower nicotine cigarettes
  - Special filters or holders
- Assisted tapering
  - QuitKey (PICS, Inc.)
    - Computer developed taper based on patient's smoking level
    - Includes telephone counseling support

NONPHARMACOLOGIC METHODS (cont'd)

- Formal cessation programs
  - Self-help programs
  - Individual counseling
  - Group programs
  - Telephone counseling
    - 1-800-QUITNOW
    - 1-800-786-8669
  - Web-based counseling
    - www.smokefree.gov
    - www.quitnet.com
    - www.becomeanex.org
- Acupuncture therapy
- Hypnotherapy
- Massage therapy

PHARMACOLOGIC METHODS: FIRST-LINE THERAPIES

Three general classes of FDA-approved drugs for smoking cessation:

- Nicotine replacement therapy (NRT)
  - Nicotine gum, patch, lozenge, nasal spray, inhaler
- Psychotropics
  - Sustained-release bupropion
- Partial nicotinic receptor agonist
  - Varenicline

PHARMACOTHERAPY

"Clinicians should encourage all patients attempting to quit to use effective medications for tobacco dependence treatment, except where contraindicated or for specific populations* for which there is insufficient evidence of effectiveness."

** Includes pregnant women, smokeless tobacco users, light smokers, and adolescents.*

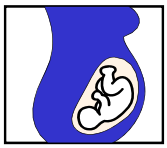
Medications significantly improve success rates.

Fiore et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline.* Rockville, MD: USDHHS, PHS, May 2008.

PHARMACOTHERAPY: USE in PREGNANCY

- The Clinical Practice Guideline makes no recommendation regarding use of medications in pregnant smokers
  - Insufficient evidence of effectiveness
- Category C: varenicline, bupropion SR
- Category D: prescription formulations of NRT

"Because of the serious risks of smoking to the pregnant smoker and the fetus, whenever possible pregnant smokers should be offered person-to-person psychosocial interventions that exceed minimal advice to quit." (p. 165)



Fiore et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline.* Rockville, MD: USDHHS, PHS, May 2008.

PHARMACOTHERAPY: OTHER SPECIAL POPULATIONS

Pharmacotherapy is **not** recommended for:

- Smokeless tobacco users
  - No FDA indication for smokeless tobacco cessation
- Individuals smoking fewer than 10 cigarettes per day
- Adolescents
  - Nonprescription sales (patch, gum, lozenge) are restricted to adults ≥18 years of age
  - NRT use in minors requires a prescription

Recommended treatment is behavioral counseling.

Fiore et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline.* Rockville, MD: USDHHS, PHS, May 2008.

NRT: RATIONALE for USE

- Reduces physical withdrawal from nicotine
- Eliminates the immediate, reinforcing effects of nicotine that is rapidly absorbed via tobacco smoke
- Allows patient to focus on behavioral and psychological aspects of tobacco cessation

NRT products approximately doubles quit rates.

NRT: PRODUCTS

Polacrilex gum
- Nicorette (OTC)
- Generic nicotine gum (OTC)

Lozenge
- Nicorette Lozenge (OTC)
- Nicorette Mini Lozenge (OTC)
- Generic nicotine lozenge (OTC)

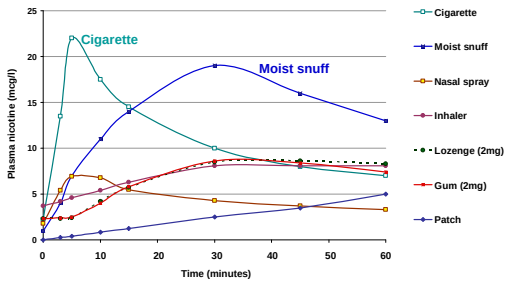
Transdermal patch
- NicoDerm CQ (OTC)
- Generic nicotine patches (OTC, Rx)

Nasal spray
- Nicotrol NS (Rx)

Inhaler
- Nicotrol (Rx)

Patients should stop using all forms of tobacco upon initiation of the NRT regimen.

PLASMA NICOTINE CONCENTRATIONS for NICOTINE-CONTAINING PRODUCTS



NRT: PRECAUTIONS

- Patients with underlying cardiovascular disease
  - Recent myocardial infarction (within past 2 weeks)
  - Serious arrhythmias
  - Serious or worsening angina

NRT products may be appropriate for these patients if they are under medical supervision.

NICOTINE GUM
Nicorette (GlaxoSmithKline); generics

- Resin complex
  - Nicotine
  - Polacrilin
- Sugar-free chewing gum base
- Contains buffering agents to enhance buccal absorption of nicotine
- Available: 2 mg, 4 mg; original, cinnamon, fruit, mint (various), and orange flavors

NICOTINE GUM: DOSING

Dosage is based on the "time to first cigarette" (TTFC) as an indicator of nicotine dependence

Use the 2 mg gum:

If you smoke your first cigarette more than 30 minutes after waking

Use the 4 mg gum:

If you smoke your first cigarette of the day within 30 minutes of waking

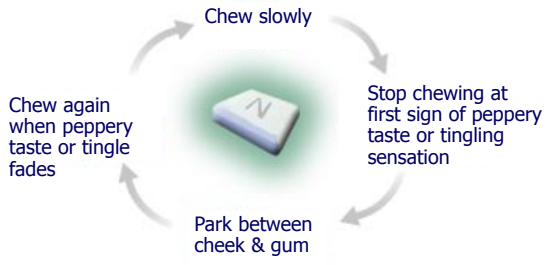
NICOTINE GUM: DOSING (cont'd)

Recommended Usage Schedule for Nicotine Gum		
Weeks 1–6	**Weeks 7–9**	**Weeks 10–12**
1 piece q 1–2 h	**1 piece q 2–4 h**	**1 piece q 4–8 h**
DO NOT USE MORE THAN 24 PIECES PER DAY.		

NICOTINE GUM: DIRECTIONS for USE

- Chew each piece very *slowly* several times
- Stop chewing at first sign of peppery taste or slight tingling in mouth (~15 chews, but varies)
- "Park" gum between cheek and gum (to allow absorption of nicotine across buccal mucosa)
- Resume slow chewing when taste or tingle fades
- When taste or tingle returns, stop and park gum in different place in mouth
- Repeat chew/park steps until most of the nicotine is gone (taste or tingle does not return; generally 30 minutes)

NICOTINE GUM: CHEWING TECHNIQUE SUMMARY



NICOTINE GUM: ADDITIONAL PATIENT EDUCATION

- To improve chances of quitting, use at least nine pieces of gum daily
- The effectiveness of nicotine gum may be reduced by some foods and beverages:
  - Coffee
  - Juices
  - Wine
  - Soft drinks

Do NOT eat or drink for 15 minutes BEFORE or while using nicotine gum.

NICOTINE GUM: ADD'L PATIENT EDUCATION (cont'd)

- Chewing gum will *not* provide same rapid satisfaction that smoking provides
- Chewing gum too rapidly can cause excessive release of nicotine, resulting in
  - Lightheadedness
  - Nausea and vomiting
  - Irritation of throat and mouth
  - Hiccups
  - Indigestion

NICOTINE GUM: ADD'L PATIENT EDUCATION (cont'd)

- Side effects of nicotine gum include
  - Mouth soreness
  - Hiccups
  - Dyspepsia
  - Jaw muscle ache
- Nicotine gum may stick to dental work
  - Discontinue use if excessive sticking or damage to dental work occurs

NICOTINE GUM: SUMMARY

ADVANTAGES

- Might satisfy oral cravings.
- Might delay weight gain (4-mg strength).
- Patients can titrate therapy to manage withdrawal symptoms.
- A variety of flavors are available.

DISADVANTAGES

- 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 might not be socially acceptable.

NICOTINE LOZENGE

Nicorette Lozenge and Nicorette Mini Lozenge (GlaxoSmithKline); generics

- Nicotine polacrilex formulation
  - Delivers ~25% more nicotine than equivalent gum dose
- Sugar-free mint, cherry flavors
- Contains buffering agents to enhance buccal absorption of nicotine
- Available: 2 mg, 4 mg

NICOTINE LOZENGE: DOSING

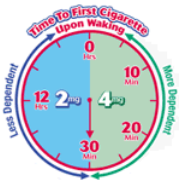
Dosage is based on the "time to first cigarette" (TTFC) as an indicator of nicotine dependence

Use the 2 mg lozenge:

If you smoke your first cigarette more than 30 minutes after waking

Use the 4 mg lozenge:

If you smoke your first cigarette of the day within 30 minutes of waking



NICOTINE LOZENGE: DOSING (cont'd)

Recommended Usage Schedule for the Nicotine Lozenge		
Weeks 1–6	**Weeks 7–9**	**Weeks 10–12**
1 lozenge q 1–2 h	**1 lozenge q 2–4 h**	**1 lozenge q 4–8 h**
DO NOT USE MORE THAN 20 LOZENGES PER DAY.		

NICOTINE LOZENGE: DIRECTIONS for USE

- Use according to recommended dosing schedule
- Place in mouth and allow to dissolve slowly (nicotine release may cause warm, tingling sensation)
- Do not chew or swallow lozenge.
- Occasionally rotate to different areas of the mouth.
- Standard lozenges will dissolve completely in about 20–30 minutes; Nicorette Mini lozenge will dissolve in 10 minutes.

NICOTINE LOZENGE: ADDITIONAL PATIENT EDUCATION

- To improve chances of quitting, use at least nine lozenges daily during the first 6 weeks
- The lozenge will *not* provide the same rapid satisfaction that smoking provides
- The effectiveness of the nicotine lozenge may be reduced by some foods and beverages:
  - Coffee
  - Juices
  - Wine
  - Soft drinks

Do NOT eat or drink for 15 minutes BEFORE or while using the nicotine lozenge.

NICOTINE LOZENGE: ADD'L PATIENT EDUCATION (cont'd)

- Side effects of the nicotine lozenge include
  - Nausea
  - Hiccups
  - Cough
  - Heartburn
  - Headache
  - Flatulence
  - Insomnia

NICOTINE LOZENGE: SUMMARY

ADVANTAGES

- Might satisfy oral cravings.
- Might delay weight gain (4-mg strength).
- Easy to use and conceal.
- Patients can titrate therapy to manage withdrawal symptoms.
- Several flavors are available.

DISADVANTAGES

- Need for frequent dosing can compromise compliance
- Gastrointestinal side effects (nausea, hiccups, and heartburn) may be bothersome.

TRANSDERMAL NICOTINE PATCH

NicoDerm CQ (GlaxoSmithKline); generic

- Nicotine is well absorbed across the skin
- Delivery to systemic circulation avoids hepatic first-pass metabolism
- Plasma nicotine levels are lower and fluctuate less than with smoking

TRANSDERMAL NICOTINE PATCH: PREPARATION COMPARISON

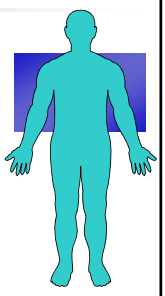
Product	NicoDerm CQ	Generic
Nicotine delivery	24 hours	24 hours
Availability	OTC	Rx/OTC
Patch strengths	7 mg 14 mg 21 mg	7 mg 14 mg 21 mg

TRANSDERMAL NICOTINE PATCH: DOSING

Product	Light Smoker	Heavy Smoker
NicoDerm CQ	**≤10 cigarettes/day** Step 2 (14 mg x 6 weeks) Step 3 (7 mg x 2 weeks)	**>10 cigarettes/day** Step 1 (21 mg x 6 weeks) Step 2 (14 mg x 2 weeks) Step 3 (7 mg x 2 weeks)
Generic (formerly Habitrol)	**≤10 cigarettes/day** Step 2 (14 mg x 6 weeks) Step 3 (7 mg x 2 weeks)	**>10 cigarettes/day** Step 1 (21 mg x 4 weeks) Step 2 (14 mg x 2 weeks) Step 3 (7 mg x 2 weeks)

TRANSDERMAL NICOTINE PATCH: DIRECTIONS for USE

- Choose an area of skin on the upper body or upper outer part of the arm
- Make sure skin is clean, dry, hairless, and not irritated
- Apply patch to different area each day
- Do not use same area again for at least 1 week

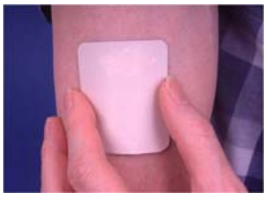


TRANSDERMAL NICOTINE PATCH: DIRECTIONS for USE (cont'd)

- Remove patch from protective pouch
- Peel off half of the backing from patch

TRANSDERMAL NICOTINE PATCH: DIRECTIONS for USE (cont'd)

- Apply adhesive side of patch to skin
- Peel off remaining protective covering
- Press firmly with palm of hand for 10 seconds
- Make sure patch sticks well to skin, especially around edges



TRANSDERMAL NICOTINE PATCH: DIRECTIONS for USE (cont'd)

- Wash hands: Nicotine on hands can get into eyes or nose and cause stinging or redness
- Do not leave patch on skin for more than 24 hours—doing so may lead to skin irritation
- Adhesive remaining on skin may be removed with rubbing alcohol or acetone
- Dispose of used patch by folding it onto itself, completely covering adhesive area

TRANSDERMAL NICOTINE PATCH: ADDITIONAL PATIENT EDUCATION

- Water will not harm the nicotine patch if it is applied correctly; patients may bathe, swim, shower, or exercise while wearing the patch
- Do *not* cut patches to adjust dose
  - Nicotine may evaporate from cut edges
  - Patch may be less effective
- Keep new and used patches out of the reach of children and pets
- Remove patch before MRI procedures

TRANSDERMAL NICOTINE PATCH: ADD'L PATIENT EDUCATION (cont'd)

- Side effects to expect in first hour:
  - Mild itching
  - Burning
  - Tingling
- Additional possible side effects:
  - Vivid dreams or sleep disturbances
  - Headache

TRANSDERMAL NICOTINE PATCH: ADD'L PATIENT EDUCATION (cont'd)

- After patch removal, skin may appear red for 24 hours
  - If skin stays red more than 4 days or if it swells or a rash appears, contact health care provider—do not apply new patch
- Local skin reactions (redness, burning, itching)
  - Usually caused by adhesive
  - Up to 50% of patients experience this reaction
  - Fewer than 5% of patients discontinue therapy
  - Avoid use in patients with dermatologic conditions (e.g., psoriasis, eczema, atopic dermatitis)

TRANSDERMAL NICOTINE PATCH: SUMMARY

ADVANTAGES

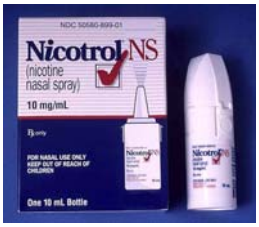
- Provides consistent nicotine levels.
- Easy to use and conceal.
- Once daily dosing associated with fewer compliance problems.

DISADVANTAGES

- Patients cannot titrate the dose to acutely manage withdrawal symptoms.
- Allergic reactions to the adhesive may occur.
- Patients with dermatologic conditions should not use the patch.

NICOTINE NASAL SPRAY
Nicotrol NS (Pfizer)

- Aqueous solution of nicotine in a 10-ml spray bottle
- Each metered dose actuation delivers
  - 50 mcL spray
  - 0.5 mg nicotine
- ~100 doses/bottle
- Rapid absorption across nasal mucosa



NICOTINE NASAL SPRAY: DOSING & ADMINISTRATION

- One dose = 1 mg nicotine
  (2 sprays, one 0.5 mg spray in **each** nostril)
- Start with 1–2 doses per hour
- Increase prn to *maximum* dosage of 5 doses per hour or 40 mg (80 sprays; ~½ bottle) daily
- For best results, patients should use at least 8 doses daily for the first 6–8 weeks
- Termination:
  - Gradual tapering over an additional 4–6 weeks

NICOTINE NASAL SPRAY: DIRECTIONS for USE

- Press in circles on sides of bottle and pull to remove cap

NICOTINE NASAL SPRAY: DIRECTIONS for USE (cont'd)

- Prime the pump (before first use)
  - Re-prime (1-2 sprays) if spray not used for 24 hours
- Blow nose (if not clear)
- Tilt head back slightly and insert tip of bottle into nostril as far as comfortable
- Breathe through mouth, and spray once in each nostril
- Do not sniff or inhale while spraying

NICOTINE NASAL SPRAY: DIRECTIONS for USE (cont'd)

- If nose runs, gently sniff to keep nasal spray in nose
- Wait 2–3 minutes before blowing nose
- Wait 5 minutes before driving or operating heavy machinery
  - Spray may cause tearing, coughing, and sneezing
- Avoid contact with skin, eyes, and mouth
  - If contact occurs, rinse with water immediately
  - Nicotine is absorbed through skin and mucous membranes

NICOTINE NASAL SPRAY: ADDITIONAL PATIENT EDUCATION

- What to expect (first week):
  - Hot peppery feeling in back of throat or nose
  - Sneezing
  - Coughing
  - Watery eyes
  - Runny nose
- Side effects should lessen over a few days
  - Regular use during the first week will help in development of tolerance to the irritant effects of the spray
- If side effects do not decrease after a week, contact health care provider

NICOTINE NASAL SPRAY: SUMMARY

ADVANTAGES

- Patients can easily titrate therapy to rapidly manage withdrawal symptoms.

DISADVANTAGES

- Need for frequent dosing can compromise compliance.
- Nasal/throat irritation may be bothersome.
- Higher dependence potential.
- Patients with chronic nasal disorders or severe reactive airway disease should not use the spray.

NICOTINE INHALER

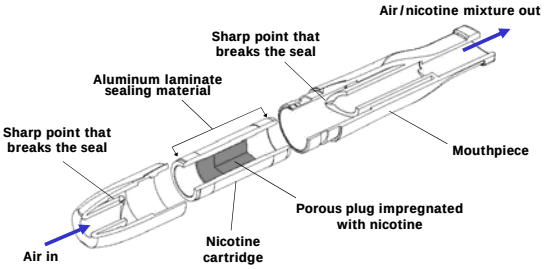
Nicotrol Inhaler (Pfizer)

- Nicotine inhalation system consists of:
  - Mouthpiece
  - Cartridge with porous plug containing 10 mg nicotine and 1 mg menthol
- Delivers 4 mg nicotine vapor, absorbed across buccal mucosa

NICOTINE INHALER: DOSING

- Start with at least 6 cartridges/day during the first 3-6 weeks of treatment
  - Increase prn to *maximum* of 16 cartridges/day
  - In general, use 1 cartridge every 1-2 hours
- Recommended duration of therapy is 3 months
- Gradually reduce daily dosage over the following 6–12 weeks

NICOTINE INHALER: SCHEMATIC DIAGRAM



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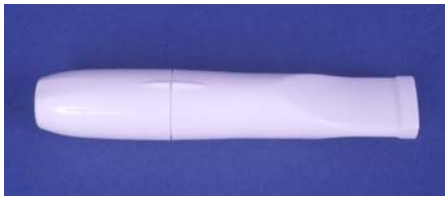
NICOTINE INHALER: DIRECTIONS for USE

- Align marks on the mouthpiece



NICOTINE INHALER: DIRECTIONS for USE (cont'd)

- Pull and separate mouthpiece into two parts

NICOTINE INHALER: DIRECTIONS for USE (cont'd)

- Press nicotine cartridge firmly into bottom of mouthpiece until seal breaks

NICOTINE INHALER: DIRECTIONS for USE (cont'd)

- Put top on mouthpiece and align marks to close
- Press down firmly to break top seal of cartridge
- Twist top to misalign marks and secure unit

NICOTINE INHALER: DIRECTIONS for USE (cont'd)

- During inhalation, nicotine is vaporized and absorbed across oropharyngeal mucosa
- Inhale into back of throat or puff in short breaths
- Nicotine in cartridges is depleted after about 20 minutes of active puffing
  - Cartridge does *not* have to be used all at once
  - Open cartridge retains potency for 24 hours
- Mouthpiece is reusable; clean regularly with mild detergent

NICOTINE INHALER: ADDITIONAL PATIENT EDUCATION

- Side effects associated with the nicotine inhaler include:
  - Mild irritation of the mouth or throat
  - Cough
  - Headache
  - Rhinitis
  - Dyspepsia
- Severity generally rated as mild, and frequency of symptoms declined with continued use

NICOTINE INHALER: ADD'L PATIENT EDUCATION (cont'd)

- The inhaler may not be as effective in very cold (<59°F) temperatures—delivery of nicotine vapor may be compromised
- Use the inhaler longer and more often at first to help control cravings (best results are achieved with frequent continuous puffing over 20 minutes)
- Effectiveness of the nicotine inhaler may be reduced by some foods and beverages

Do NOT eat or drink for 15 minutes BEFORE or while using the nicotine inhaler.

NICOTINE INHALER: SUMMARY

ADVANTAGES

- Patients can easily titrate therapy to manage withdrawal symptoms.
- The inhaler mimics the hand-to-mouth ritual of smoking.

DISADVANTAGES

- 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 the inhaler with caution.

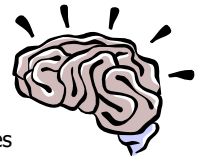
BUPROPION SR

Zyban (GlaxoSmithKline); generic

- Nonnicotine cessation aid
- Sustained-release antidepressant
- Oral formulation

BUPROPION: MECHANISM of ACTION

- Atypical antidepressant thought to affect levels of various brain neurotransmitters
  - Dopamine
  - Norepinephrine
- Clinical effects
  - ↓ craving for cigarettes
  - ↓ symptoms of nicotine withdrawal



BUPROPION: PHARMACOKINETICS

Absorption
- Bioavailability: 5–20%

Metabolism
- Undergoes extensive hepatic metabolism (CYP2B6)

Elimination
- Urine (87%) and feces (10%)

Half-life
- Bupropion (21 hours); metabolites (20–37 hours)

BUPROPION: CONTRAINDICATIONS

- Patients with a seizure disorder
- Patients taking
  - Wellbutrin, Wellbutrin SR, Wellbutrin XL
  - MAO inhibitors in preceding 14 days
- Patients with a current or prior diagnosis of anorexia or bulimia nervosa
- Patients undergoing abrupt discontinuation of alcohol or sedatives (including benzodiazepines)

BUPROPION: WARNINGS and PRECAUTIONS

- Neuropsychiatric symptoms and suicide risk
  - Changes in mood (depression and mania)
  - Psychosis/hallucinations/paranoia/delusions
  - Homicidal ideation/hostility
  - Agitation/anxiety/panic
  - Suicidal ideation or attempts
  - Completed suicide

Patients should stop bupropion and contact a health care provider immediately if agitation, hostility, depressed mood or changes in thinking or behavior (including suicidal ideation) are observed

BUPROPION: WARNINGS and PRECAUTIONS (cont'd)

Bupropion should be used with caution in the following populations:

- Patients with a history of seizure
- Patients with a history of cranial trauma
- Patients taking medications that lower the seizure threshold (antipsychotics, antidepressants, theophylline, systemic steroids)
- Patients with severe hepatic cirrhosis
- Patients with depressive or psychiatric disorders

BUPROPION SR: DOSING

Patients should begin therapy 1 to 2 weeks PRIOR to their quit date to ensure that therapeutic plasma levels of the drug are achieved.

Initial treatment

- 150 mg po q AM x 3 days

Then…

- 150 mg po bid
- Duration, 7–12 weeks

BUPROPION: ADVERSE EFFECTS

Common side effects include the following:

- Insomnia (avoid bedtime dosing)
- Dry mouth

Less common but reported effects:

- Tremor
- Skin rash

BUPROPION: ADDITIONAL PATIENT EDUCATION

- Dose tapering not necessary when discontinuing treatment
- If no significant progress toward abstinence by seventh week, therapy is unlikely to be effective
  - Discontinue treatment
  - Reevaluate and restart at later date

BUPROPION SR: SUMMARY

ADVANTAGES

- Easy to use oral formulation.
- Twice daily dosing might reduce compliance problems.
- Might delay weight gain
- Bupropion might be beneficial for patients with depression.

DISADVANTAGES

- The seizure risk is increased.
- Several contraindications and precautions preclude use in some patients.

VARENICLINE
Chantix (Pfizer)

- Nonnicotine cessation aid
- Partial nicotinic receptor agonist
- Oral formulation

VARENICLINE: MECHANISM of ACTION

- Binds with high affinity and selectivity at $\alpha_4\beta_2$ neuronal nicotinic acetylcholine receptors
  - Stimulates low-level agonist activity
  - Competitively inhibits binding of nicotine
- Clinical effects
  - ↓ symptoms of nicotine withdrawal
  - Blocks dopaminergic stimulation responsible for reinforcement & reward associated with smoking

VARENICLINE: PHARMACOKINETICS

Absorption

- Virtually complete after oral administration; not affected by food

Metabolism

- Undergoes minimal metabolism

Elimination

- Primarily renal through glomerular filtration and active tubular secretion; 92% excreted unchanged in urine

Half-life

- 24 hours

VARENICLINE: WARNINGS and PRECAUTIONS

- Neuropsychiatric Symptoms and Suicidality
  - Changes in mood (depression and mania)
  - Psychosis/hallucinations/paranoia/delusions
  - Homicidal ideation/hostility
  - Agitation/anxiety/panic
  - Suicidal ideation or attempts
  - Completed suicide

Patients should stop varenicline and contact a health care provider immediately if agitation, hostility, depressed mood or changes in thinking or behavior (including suicidal ideation) are observed

VARENICLINE: WARNINGS and PRECAUTIONS (cont'd)

- Cardiovascular adverse events in patients with existing cardiovascular disease
- Hypersensitivity reactions
- Serious skin reactions
- Accidental injury
- Nausea

VARENICLINE: DOSING

Patients should begin therapy 1 week PRIOR to their quit date. The dose is gradually increased to minimize treatment-related nausea and insomnia.

Initial dose titration

Treatment Day	Dose
Day 1 to day 3	0.5 mg qd
Day 4 to day 7	0.5 mg bid
Day 8 to end of treatment*	1 mg bid

* Up to 12 weeks

VARENICLINE: ADVERSE EFFECTS

- Common (≥5% and 2-fold higher than placebo)
  - Nausea
  - Sleep disturbances (insomnia, abnormal dreams)
  - Constipation
  - Flatulence
  - Vomiting

VARENICLINE: ADDITIONAL PATIENT EDUCATION

- Doses should be taken after eating, with a full glass of water
- Nausea and insomnia are usually temporary side effects
  - If symptoms persist, notify your health care provider
- May experience vivid, unusual or strange dreams during treatment
- Use caution driving or operating machinery until effects of quitting smoking with varenicline are known

VARENICLINE: ADDITIONAL PATIENT EDUCATION (cont'd)

- Stop taking varenicline and contact a health-care provider immediately if agitation, depressed mood, suicidal thoughts or changes in behavior are noted
- Stop taking varenicline at the first sign of rash with mucosal lesions and contact a health-care provider immediately
- Discontinue varenicline and seek immediate medical care if swelling of the face, mouth (lip, gum, tongue) and neck are noted

VARENICLINE: SUMMARY

ADVANTAGES

- Easy to use oral formulation.
- Twice daily dosing might reduce compliance problems.
- Offers a new mechanism of action for persons who have failed other agents.

DISADVANTAGES

- May induce nausea in up to one third of patients.
- Post-marketing surveillance data indicate potential for neuropsychiatric symptoms.

PHARMACOLOGIC METHODS: SECOND-LINE THERAPIES

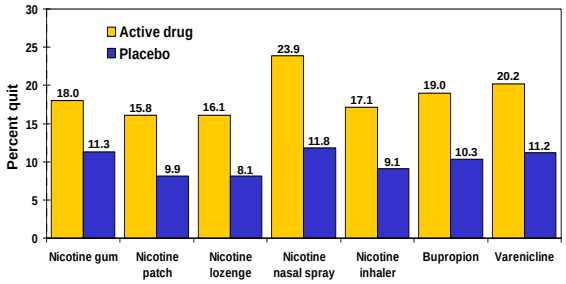
- Clonidine (Catapres transdermal or oral)
- Nortriptyline (Pamelor oral)

HERBAL DRUGS for SMOKING CESSATION

- Lobeline
  - Derived from leaves of Indian tobacco plant (*Lobelia inflata*)
  - Partial nicotinic agonist
  - No scientifically rigorous trials with long-term follow-up
  - No evidence to support use for smoking cessation

Illustration courtesy of Missouri Botanical Garden ©1995-2005. http://www.illustratedgarden.org/

LONG-TERM (≥6 month) QUIT RATES for AVAILABLE CESSATION MEDICATIONS



Data adapted from Cahill et al. (2008). *Cochrane Database Syst Rev;* Stead et al. (2008). *Cochrane Database Syst Rev;* Hughes et al. (2007). *Cochrane Database Syst Rev*

COMBINATION PHARMACOTHERAPY

Regimens with enough evidence to be 'recommended' first-line

- **Combination NRT**

  Long-acting formulation (patch)
  - Produces relatively constant levels of nicotine

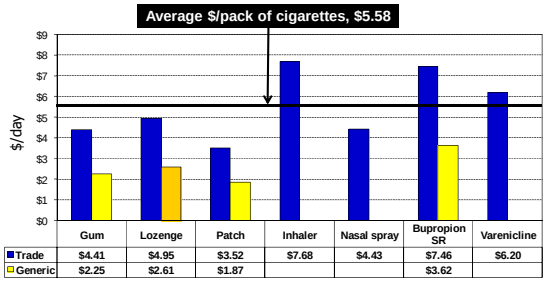
  PLUS

  Short-acting formulation (gum, inhaler, nasal spray)
  - Allows for acute dose titration as needed for nicotine withdrawal symptoms
- **Bupropion SR + Nicotine Patch**

COMPLIANCE IS KEY to QUITTING

- Promote compliance with prescribed regimens.
- Use according to dosing schedule, NOT as needed.
- Consider telling the patient:
  - "When you use a cessation product it is important to read all the directions thoroughly before using the product. The products work best in alleviating withdrawal symptoms when used correctly, and according to the recommended dosing schedule."

COMPARATIVE DAILY COSTS of PHARMACOTHERAPY



	Gum	Lozenge	Patch	Inhaler	Nasal spray	Bupropion SR	Varenicline
Trade	$4.41	$4.95	$3.52	$7.68	$4.43	$7.46	$6.20
Generic	$2.25	$2.61	$1.87			$3.62	

SUMMARY

- To maximize success, interventions should include counseling and one or more medications
- Clinicians should encourage the use of effective medications by all patients attempting to quit smoking
  - Exceptions include medical contraindications or use in specific populations for which there is insufficient evidence of effectiveness
- First-line medications that reliably increase long-term smoking cessation rates include:
  - Bupropion SR
  - Nicotine replacement therapy (gum, inhaler, lozenge, patch, nasal spray)
  - Varenicline
- Use of effective combinations of medications should be considered