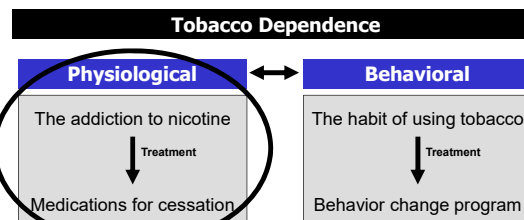




MEDICATIONS for CESSATION



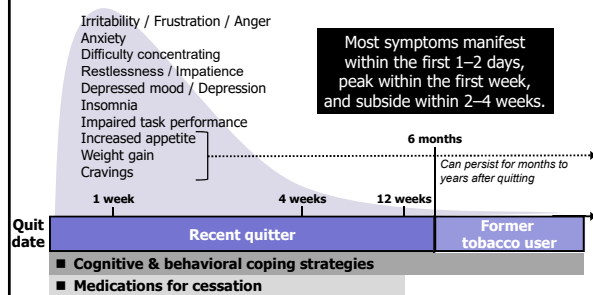
TOBACCO DEPENDENCE: A 2-PART PROBLEM



Treatment should address the physiological **and** the behavioral aspects of dependence.



NICOTINE WITHDRAWAL SYMPTOMS: Time Course* and Management



*Timeline aspect of the figure is not according to scale.

Data from Hughes. (2007). *Nicotine Tob Res* 9:315-327.



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 SPECIAL POPULATIONS

Pharmacotherapy is **not** recommended for:

- Pregnant smokers
 - Insufficient evidence of effectiveness
- Smokeless tobacco users
 - No FDA indication for smokeless tobacco cessation
- Individuals smoking fewer than 10 cigarettes per day
- Adolescents
 - Nonprescription sales of nicotine replacement therapy (NRT) products (i.e., patch, gum, lozenge) are restricted to adults ≥18 years of age
 - NRT use in minors requires a prescription

Recommended treatment is behavioral counseling.



FDA-APPROVED MEDICATIONS for CESSATION

Nicotine polacrilex gum*

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

Nicotine lozenge*

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

Nicotine transdermal patch*

- NicoDerm CQ (OTC)
- Generic nicotine patches (OTC)

Nicotine inhaler *

- Nicotrol (Rx)

Nicotine nasal spray *

- Nicotrol NS (Rx)

Bupropion SR

- Generic (Rx)

Varenicline

- Chantix (Rx)

* Nicotine replacement therapy (NRT) products.



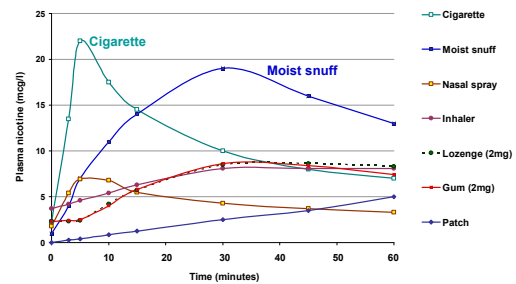
NICOTINE REPLACEMENT THERAPY (NRT) RATIONALE for USE

- 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.



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; generics

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



NICOTINE LOZENGE Nicorette Lozenge and Nicorette Mini Lozenge; 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 GUM & LOZENGE: DOSING

Dose based on the “time to first cigarette” (TTFC) as an indicator of nicotine dependence

Use the 2 mg gum/lozenge:

If first cigarette of the day is smoked more than 30 minutes after waking

Use the 4 mg gum/lozenge:

If first cigarette of the day is smoked within 30 minutes of waking





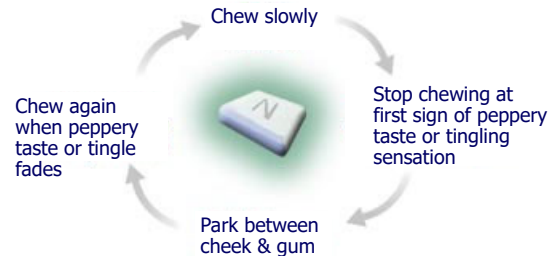
NICOTINE GUM & LOZENGE: DOSING (cont'd)

Recommended Usage Schedule		
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 of GUM
or 20 LOZENGES per day.**



NICOTINE GUM: DIRECTIONS FOR USE



NICOTINE LOZENGE: DIRECTIONS for USE

- Place in mouth and allow to dissolve slowly (nicotine release may cause warm, tingling sensation)
- Do not chew or swallow
- Occasionally rotate to different areas of the mouth
- Lozenges will dissolve completely in about 20–30 minutes



NICOTINE GUM/LOZENGE: ADDITIONAL PATIENT EDUCATION

- To improve chances of quitting, use at least nine pieces daily during the first 6 weeks
- The gum/lozenge will *not* provide the same rapid satisfaction that smoking provides
- The effectiveness of the nicotine gum/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 gum or lozenge.



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

- Chewing the lozenge or using incorrect gum chewing technique can cause excessive and rapid release of nicotine, resulting in:
 - Lightheadedness/dizziness
 - Nausea and vomiting
 - Hiccups
 - Irritation of throat and mouth



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

- Adverse effects of nicotine gum and lozenge:
 - Mouth and throat irritation
 - Hiccups
 - Gastrointestinal complaints (dyspepsia, nausea)
- Adverse effects associated with nicotine gum:
 - Jaw muscle ache
 - May stick to dental work



NICOTINE GUM/LOZENGE: SUMMARY

ADVANTAGES

- Might serve as an oral substitute for tobacco
- Might delay weight gain
- Can be titrated to manage withdrawal symptoms
- Can be used in combination with other agents to manage situational urges
- Relatively inexpensive

DISADVANTAGES

- Need for frequent dosing can compromise adherence
- Gastrointestinal adverse effects (nausea, hiccups, and dyspepsia) may be bothersome
- Specific to nicotine gum:
 - Might be problematic for patients with significant dental work
 - Proper chewing technique is necessary for effectiveness and to minimize adverse effects
 - Chewing might not be acceptable or desirable for some patients



TRANSDERMAL NICOTINE PATCH NicoDerm CQ; generic

- Continuous (24-hour) nicotine delivery system
- Nicotine is well absorbed across the skin
- Transdermal delivery to systemic circulation avoids hepatic first-pass metabolism
- Plasma nicotine levels are lower and fluctuate less than with smoking



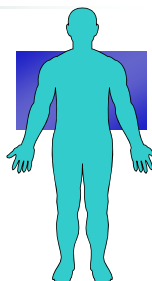
TRANSDERMAL NICOTINE PATCH: DOSING

Product	Light Smoker	Heavy Smoker
NicoDerm CQ	≤10 cigarettes/day	>10 cigarettes/day
	Step 2 (14 mg x 6 weeks)	Step 1 (21 mg x 6 weeks)
	Step 3 (7 mg x 2 weeks)	Step 2 (14 mg x 2 weeks)
Generic	≤10 cigarettes/day	>10 cigarettes/day
	Step 2 (14 mg x 6 weeks)	Step 1 (21 mg x 4 weeks)
	Step 3 (7 mg x 2 weeks)	Step 2 (14 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 protective liner and 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
 - Can unpredictably effect nicotine delivery
 - 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)

Common adverse effects include:

- Irritation at the patch application site (generally within the first hour)
 - Mild itching
 - Burning
 - Tingling
- Sleep disturbances
 - Abnormal or vivid dreams
 - Insomnia



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

- Once-daily dosing associated with fewer adherence problems
- Of all NRT products, its use is least obvious to others
- Can be used in combination with other agents; delivers consistent nicotine levels over 24 hrs
- Relatively inexpensive

DISADVANTAGES

- When used as monotherapy, cannot be titrated to acutely manage withdrawal symptoms
- Not recommended for use by patients with dermatologic conditions (e.g., psoriasis, eczema, atopic dermatitis)

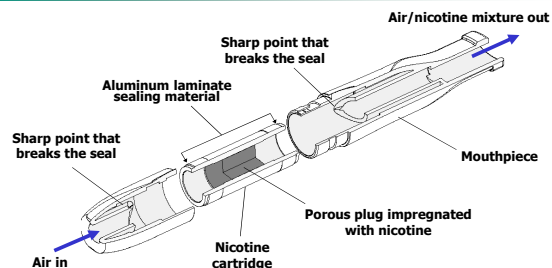


NICOTINE INHALER Nicotrol Inhaler

- 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: SCHEMATIC DIAGRAM



Reprinted with permission from Schneider et al. (2001). *Clinical Pharmacokinetics* 40:661-684. Adis International, Inc.



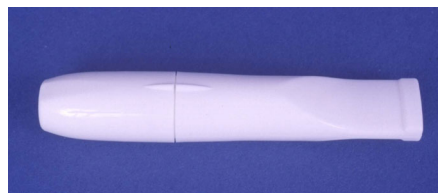
NICOTINE INHALER: DOSING

- Initial treatment (up to 12 weeks)
 - 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
- Gradually reduce daily dosage over the following 6–12 weeks
- Recommended maximum duration of therapy is 6 months



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 it pops down into place
- Line up the markings on the mouthpiece again and push the two pieces back together so they fit tightly
- 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—try different schedules (e.g., 5 minutes at a time) to find what works best
 - Open cartridge retains potency for 24 hours
- Mouthpiece is reusable; clean regularly with mild detergent



NICOTINE INHALER: ADDITIONAL PATIENT EDUCATION

- Adverse effects associated with the nicotine inhaler include:
 - Mild irritation of the mouth or throat
 - Cough
 - Hiccups
 - Gastrointestinal complaints (dyspepsia, nausea)
- Severity generally rated as mild, and frequency of symptoms declined with continued use



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

- Use inhaler at room temperature ($>60^{\circ}\text{F}$); in cold environments, the 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

- Might serve as an oral substitute for tobacco
- Can be titrated to manage withdrawal symptoms
- Mimics the hand-to-mouth ritual of smoking
- Can be used in combination with other agents to manage situational urges

DISADVANTAGES

- Need for frequent dosing can compromise adherence
- Cartridges might be less effective in cold environments ($\leq 60^{\circ}\text{F}$)
- Cost of treatment



NICOTINE NASAL SPRAY Nicotrol NS

- 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 as needed to maximum dosage of 5 doses per hour or 40 mg (80 sprays; $\sim 1/2$ bottle) daily
- At least 8 doses daily for the first 6–8 weeks
- Termination:
 - Gradual tapering over an additional 4–6 weeks
 - Recommended maximum duration of therapy is 3 months



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
- 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
- Adverse 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 adverse effects persist after a week, contact health care provider and consider alternative treatment



NICOTINE NASAL SPRAY: SUMMARY

ADVANTAGES

- Can be titrated to rapidly manage withdrawal symptoms
- Can be used in combination with other agents to manage situational urges

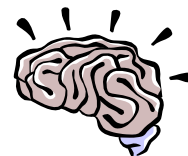
DISADVANTAGES

- Need for frequent dosing can compromise adherence
- Nasal administration might not be acceptable/desirable for some patients; nasal irritation often problematic
- Not recommended for use by patients with chronic nasal disorders or severe reactive airway disease
- Cost of treatment



BUPROPION SR: Generics

- Non-nicotine cessation aid
- 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 with a current or prior diagnosis of bulimia or anorexia nervosa
- Patients undergoing abrupt discontinuation of alcohol, benzodiazepines, barbiturates and antiepileptic drugs
- Patients taking MAO inhibitors (within 14 days of initiating or discontinuing therapy)



BUPROPION: WARNINGS and PRECAUTIONS

Bupropion should be used with caution in the following populations:

- Patients with an elevated risk for seizures, including:
 - Severe head injury
 - Concomitant use of medications that lower the seizure threshold (e.g., other bupropion products, antipsychotics, tricyclic antidepressants, theophylline)
 - Severe hepatic impairment
- Patients with underlying neuropsychiatric conditions

For a comprehensive listing of warnings and precautions, refer to the manufacturer's prescribing information.



BUPROPION: WARNINGS and PRECAUTIONS (cont'd)

- Neuropsychiatric symptoms and suicide risk
 - Changes in mood (including depression and mania)
 - Psychosis/hallucinations/paranoia/delusions
 - Homicidal ideation
 - Aggression/hostility/anxiety/panic
 - Suicidal ideation, suicide attempt, completed suicide

FDA
boxed
warning
removed
Dec 2016

Advise patients to stop taking bupropion SR and contact a health care provider immediately if symptoms such as agitation, depressed mood, or changes in behavior or thinking that are not typical are observed or if the patient develops suicidal ideation or suicidal behavior.



BUPROPION SR: DOSING

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

Initial treatment

- 150 mg po q AM for 3 days

Then...

- 150 mg po bid for 7–12 weeks
- Doses must be administered at least 8 hours apart
- Tapering not necessary when discontinuing therapy



BUPROPION: ADVERSE EFFECTS

Common adverse effects include the following:

- Insomnia (avoid bedtime dosing)
- Dry mouth
- Nausea

Less common but reported effects:

- Anxiety/difficulty concentrating
- Constipation
- Tremor
- Skin rash



BUPROPION SR: SUMMARY

ADVANTAGES

- Oral dosing is simple and associated with fewer adherence problems
- Might delay weight gain
- Bupropion might be beneficial in patients with depression
- Can be used in combination with NRT agents
- Relatively inexpensive (generic formulations)

DISADVANTAGES

- Seizure risk is increased
- Several contraindications and precautions preclude use in some patients
- Patients should be monitored for neuropsychiatric symptoms



VARENICLINE Chantix

- 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 (~90%) 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 suicide risk
 - Changes in mood (including depression and mania)
 - Psychosis/hallucinations/paranoia/delusions
 - Homicidal ideation
 - Aggression/hostility/anxiety/panic
 - Suicidal ideation, suicide attempt, completed suicide

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Dec 2016

Advise patients to stop taking varenicline and contact a health care provider immediately if symptoms such as agitation, depressed mood, or changes in behavior or thinking that are not typical are observed or if the patient develops suicidal ideation or suicidal behavior.



VARENICLINE: WARNINGS and PRECAUTIONS (cont'd)

In some patients, use of varenicline has been associated with:

- Seizures
- Enhanced effects of alcohol
- Accidental injury
- Cardiovascular events
- Somnambulism
- Angioedema and hypersensitivity reactions
- Serious skin reactions

These are rare events and most have not been causally linked to varenicline use.



VARENICLINE: STANDARD DOSING

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

	Treatment Day	Dose
Initial dose titration	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 QUIT APPROACHES



FIXED QUIT approach

- Set quit date for 1 week after starting varenicline
- Continue treatment for 12 weeks

FLEXIBLE QUIT approach

- Start taking varenicline and pick a quit date between 8 to 35 days from treatment initiation
- Continue treatment for 12 weeks

GRADUAL QUIT approach

- Start taking varenicline and reduce smoking by 50% within the first 4 weeks, an additional 50% in the next 4 weeks, and continue until complete abstinence by 12 weeks

Images from: <https://www.pfizerpro.com/product/chantix/hcp/quit-approaches>



VARENICLINE: ADVERSE EFFECTS

Common adverse effects include the following:

- Nausea
- Insomnia
- Abnormal dreams
- Headache

Less common adverse effects:

- Gastrointestinal (flatulence, constipation)
- Taste alteration



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, drinking alcohol, and operating machinery until effects of quitting smoking with varenicline are known



VARENICLINE: SUMMARY

ADVANTAGES

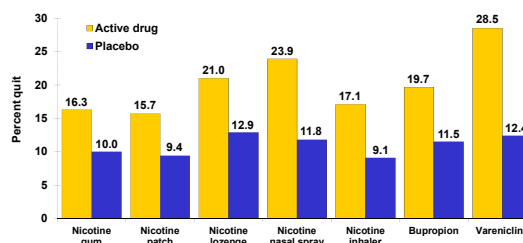
- Oral dosing is simple and associated with fewer adherence problems
- Offers a different mechanism of action for persons who have failed other agents
- Most effective agent for cessation when used as monotherapy

DISADVANTAGES

- Cost of treatment
- Patients should be monitored for potential neuropsychiatric symptoms



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



Data adapted from Hartmann-Boyce et al. (2018). *Cochrane Database Syst Rev*; Cahill et al. (2016). *Cochrane Database Syst Rev*; Hughes et al. (2014). *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, lozenge, nasal spray)

- Allows for acute dose titration as needed for nicotine withdrawal symptoms

■ Bupropion SR + Nicotine Patch



TREATMENT OPTIONS

Multiple Treatment Comparison Meta-Analysis

Comparison	Odds ratio (95% CI)
Nicotine gum vs Placebo	1.7 (1.5–1.9)
Bupropion SR vs Placebo	1.9 (1.6–2.1)
Nicotine patch vs Placebo	1.9 (1.7–2.1)
Other NRT* vs Placebo	2.0 (1.8–2.4)
Combination NRT vs Placebo	2.7 (2.1–3.7)
Varenicline vs Placebo	2.9 (2.4–3.5)

*Includes nicotine nasal spray, lozenge, and inhaler

Strong evidence that combination NRT and varenicline are more effective than bupropion SR or NRT monotherapy

Cahill et al. (2013). *Cochrane Database Syst Rev* 5:CD009329.



COMBINATION NRT: TREATMENT REGIMENS

- **Nicotine patch**
Dose: 21 mg/day x 4–6 wks → 14 mg/day x 2 wks → 7 mg/day x 2 wks
- **PLUS**
- **Nicotine gum or lozenge** (2 mg/4 mg; based on TTFC)
Dose: Use 1 piece q 1–2 hours as needed (use at least 4–5/day)
- **OR**
- **Nicotine inhaler** (10 mg cartridge; delivers 4 mg nicotine vapor)
Dose: Use 1 cartridge q 1–2 hours as needed
- **OR**
- **Nicotine nasal spray** (0.5 mg/spray)
Dose: Use 1 spray in each nostril q 1–2 hours as needed



IDENTIFY KEY ISSUES to STREAMLINE PRODUCT SELECTION*

- Do you prefer a prescription or nonprescription medication?
- Would it be a challenge for you to take a medication frequently throughout the day (e.g., a minimum of 9 times)?
 - With the exception of the nicotine patch, all NRT formulations require frequent dosing throughout the day.
 - If patient is unable to adhere to the recommended dosing, these products should be ruled out as monotherapy because they will be ineffective.

Asking these two questions will significantly reduce the time required for product selection.

* Product-specific screening—for warnings, precautions, contraindications, and personal preferences—is also essential.



"Drugs don't work..."

...in patients who don't take them."

C. Everett Koop, M.D., former U.S. Surgeon General



Medication adherence should be addressed at each encounter.



ADHERENCE IS KEY to QUITTING

- Promote adherence with prescribed regimens
 - Daily use (use according to dosing schedule, NOT as needed)
 - Full duration of treatment regimen
- Consider telling the patient:
 - "If used properly, the medicines can make you more comfortable while you are quitting."
 - "Medicines for quitting work best if you take them on a regular schedule, to **prevent** withdrawal symptoms before they occur. If you wait until you're already craving a cigarette, it will be too late. The medicines don't work as quickly as inhaled nicotine from a cigarette."



ADHERENCE IS KEY to QUITTING (cont'd)

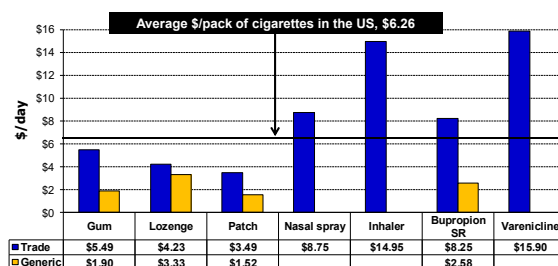
When providing medication counseling, it is important to emphasize three key facets of adherence:

- Correct strength of medication
- Taken daily, according to a fixed schedule
- Taken for the full duration of therapy

At each encounter, assess withdrawal and adjust treatment as needed.



COMPARATIVE DAILY COSTS of PHARMACOTHERAPY



*Wholesale acquisition cost from Red Book Online, Thomson Reuters, January 2019



SUMMARY

- To maximize success, interventions should include behavioral counseling and one or more medications
- Encourage the use of effective medications by all patients attempting to quit smoking
 - Exceptions include medical contraindications or 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 (as monotherapy or combination therapy)
 - Varenicline
- Varenicline and combination NRT approaches demonstrate the highest level of efficacy