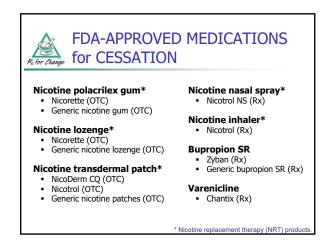


PHARMACOTHERAPY: Refor Change Use in SPECIAL POPULATIONS

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 (patch, gum, lozenge) are restricted to adults ≥18 years of age
 - NRT use in minors requires a prescription

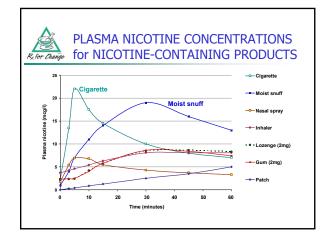
Recommended treatment is behavioral counseling.

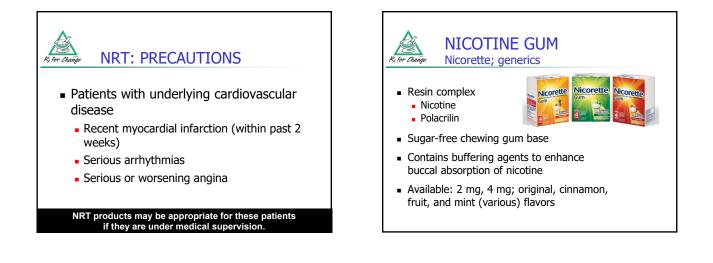


NICOTINE REPLACEMENT THERAPY (NRT) **RATIONALE for USE** Ry for Change

- 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.







Available: 2 mg, 4 mg



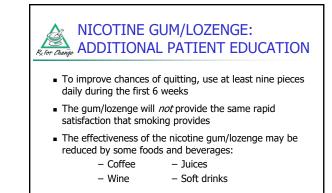


NICOTINE GUM & LOZENGE: <i>R. for Change</i> DOSING (cont'd)					
	Recommended Usage Schedule				
	Weeks 1–6	Weeks 7–9	Weeks 10-12		
	1 piece q 1–2 h	1 piece q 2–4 h	1 piece q 4–8 h		
Do not use more than 24 pieces of GUM or 20 LOZENGES per day.					



NICOTINE LOZENGE: Stor Change 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

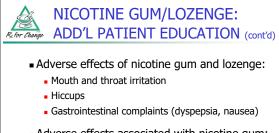


Do NOT eat or drink for 15 minutes BEFORE or while using the nicotine gum or lozenge.



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
 - Indigestion



- Adverse effects associated with <u>nicotine gum</u>:
 - Jaw muscle ache
 - May stick to dental work



NICOTINE GUM/LOZENGE: SUMMARY

ADVANTAGES

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

DISADVANTAGES

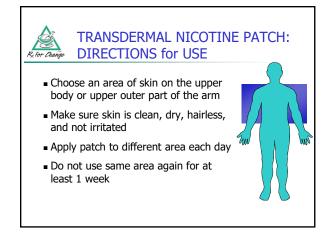
- Need for frequent dosing can compromise adherence
- Gastrointestinal adverse effects (nausea, hiccups, and dyspepsia) may be bothersome
- Specific to nicotine gum: – Might be problematic for patients with significant dental work
- Proper chewing technique is necessary for effectiveness and to minimize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

K. for Change 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





Product	Light Smoker	Heavy Smoker
	≤10 cigarettes/day	>10 cigarettes/day
Nice Down CO	Step 2 (14 mg x 6 weeks)	Step 1 (21 mg x 6 weeks)
NicoDerm CQ	Step 3 (7 mg x 2 weeks)	Step 2 (14 mg x 2 weeks)
		Step 3 (7 mg x 2 weeks)
	≤10 cigarettes/day	>10 cigarettes/day
Generic	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)
		Step 3 (7 mg x 2 weeks)



Refer Change 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



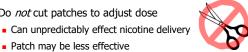


- Do not leave patch on skin for more than 24 hours doing so may lead to skin irritation
- Adhesive remaining on skin may be removed with rubbing alcohol or acetone
- Dispose of used patch by folding it onto itself, completely covering adhesive area

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

Patch may be less effective



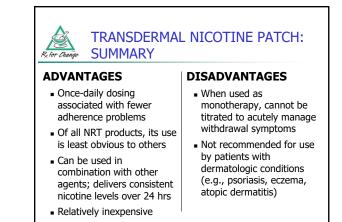
- Keep new and used patches out of the reach of children and pets
- Remove patch before MRI procedures

TRANSDERMAL NICOTINE PATCH: ADD'L PATIENT EDUCATION (cont'd) Common adverse effects include:

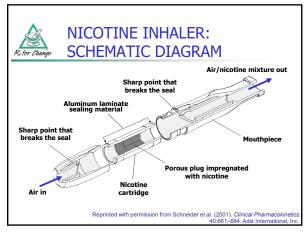
- Irritation at the patch application site (generally within the first hour)
 - Mild itching
 - Burning
 - Tingling
- Sleep disturbances
 - Abnormal or vivid dreams
- Insomnia

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)

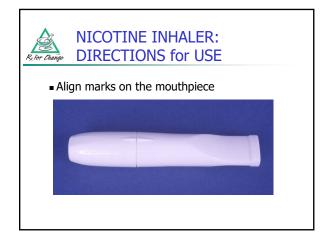








- Initial treatment (up to 12 weeks)
 - Start with at least 6 cartridges/day during the first 3–6 weeks of treatment
 - Increase prn to maximum of 16 cartridges/day
 - In general, use 1 cartridge every 1–2 hours
- Gradually reduce daily dosage over the following 6–12 weeks
- Recommended maximum duration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







 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)

Ż

R for Chang

- 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



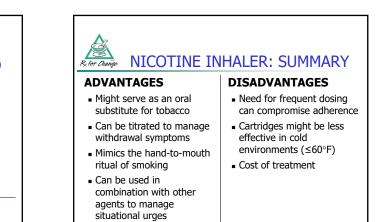
- Adverse effects associated with the nicotine inhaler include:
 - Mild irritation of the mouth or throat
 - Cough
 - Hiccups
 - Gastrointestinal complaints (dyspepsia, nausea)
- Severity generally rated as mild, and frequency of symptoms declined with continued use



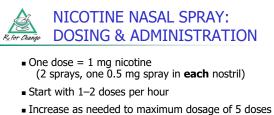
NICOTINE INHALER: ADD'L PATIENT EDUCATION (cont'd)

- Use inhaler at room temperature (>60°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.

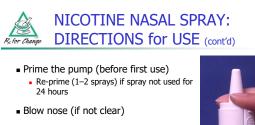






- \blacksquare Increase as needed to maximum dosage of 5 doses per hour or 40 mg (80 sprays; $\sim\!\!1\!\!2$ bottle) daily
- At least 8 doses daily for the first 6–8 weeks
- Termination:
 - Gradual tapering over an additional 4–6 weeks
 - Recommended maximum duration of therapy is 3 months





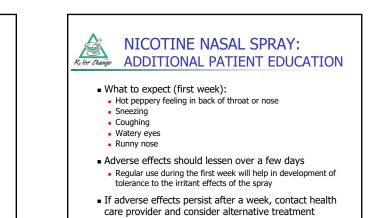
- Tilt head back slightly and insert tip of bottle into nostril as far as comfortable
- Breathe through mouth, and spray once in each nostril
- Do not sniff or inhale while spraying

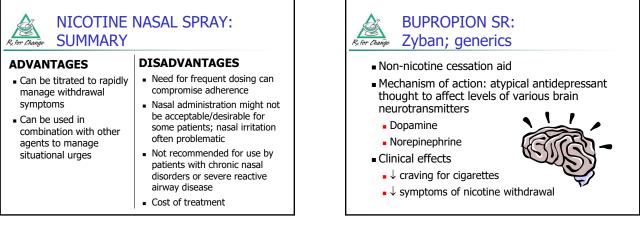




NICOTINE NASAL SPRAY: DIRECTIONS for USE (cont'd)

- 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





BUPROPION: PHARMACOKINETICS

Absorption

Bioavailability: 5–20%

Metabolism

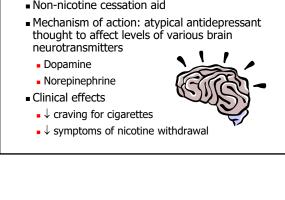
Undergoes extensive hepatic metabolism (CYP2B6)

Elimination

Urine (87%) and feces (10%)

Half-life

Bupropion (21 hours); metabolites (20–37 hours)





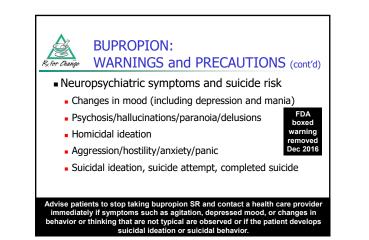
- Patients with a seizure disorder
- Patients with a current or prior diagnosis of bulimia or anorexia nervosa
- Patients undergoing abrupt discontinuation of alcohol, benzodiazepines, barbiturates and antiepileptic drugs
- Patients taking MAO inhibitors (within 14 days of initiating or discontinuing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

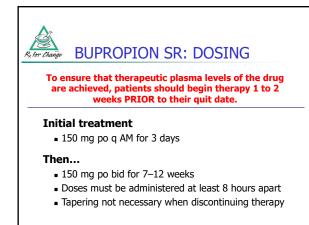


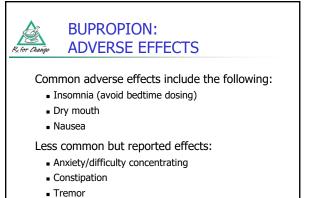
BUPROPION: WARNINGS and PRECAUTIONS

Bupropion should be used with caution in the following populations:

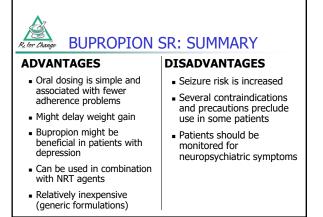
- Patients with an elevated risk for seizures, including:
 - Severe head injury
 - Concomitant use of medications that lower the seizure threshold (e.g., other bupropion products, antipsychotics, tricyclic antidepressants, theophylline)
 - Severe hepatic impairment
- Patients with underlying neuropsychiatric conditions
- For a comprehensive listing of warnings and precautions, refer to the manufacturer's prescribing information

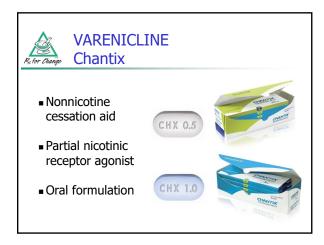






Skin rash







VARENICLINE: MECHANISM of ACTION

- \bullet 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

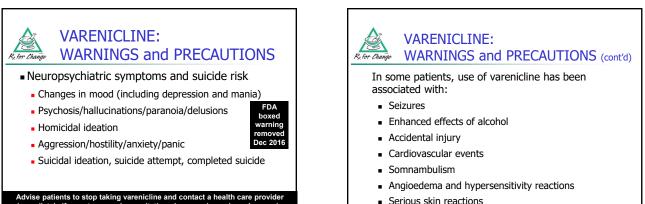
Undergoes minimal metabolism

Elimination

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

Half-life

24 hours



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: STANDARD

Patients should begin therapy 1 week PRIOR to their

quit date. The dose is gradually increased to minimize

treatment-related nausea and insomnia.

DOSING

Treatment Day

Day 1 to day 3

Day 4 to day 7

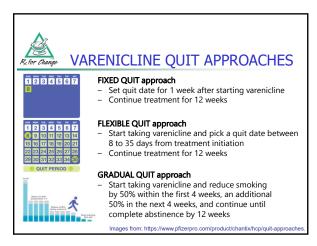
Day 8 to end of treatment*

R for Chan

Initial

dose

titration



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

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Dose

0.5 mg qd

0.5 mg bid

1 mg bid

Up to 12 week

CHX 0.5

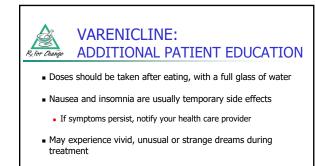
CHX 0.5 CHX 0.5

CHX 1.0 CHX 1.0

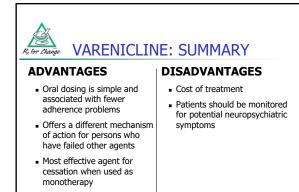
VARENICLINE: ADVERSE EFFECTS

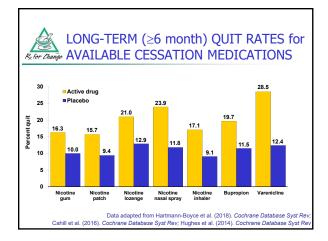
Common adverse effects include the following:

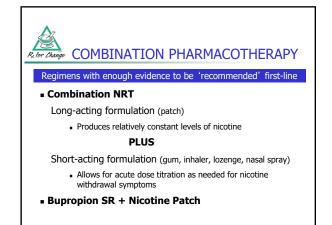
- Nausea
- Insomnia
- Abnormal dreams
- Headache
- Less common adverse effects:
 - Gastrointestinal (flatulence, constipation)
 - Taste alteration

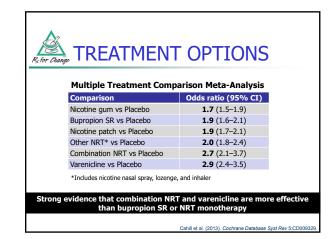


 Use caution driving, drinking alcohol, and operating machinery until effects of quitting smoking with varenicline are known





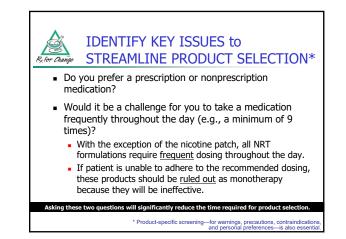




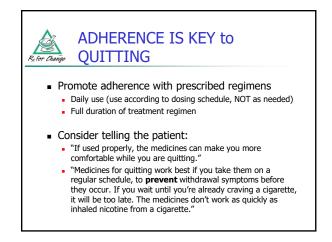


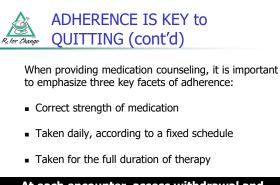
Dose: 21 mg/day x 4–6 wks \rightarrow 14 mg/day x 2 wks \rightarrow 7 mg/day x 2 wks **PLUS**

- 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

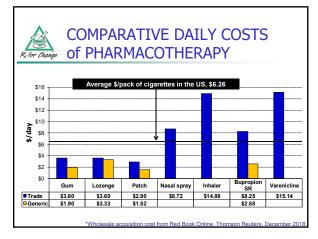








At each encounter, assess withdrawal and adjust treatment as needed.



Refor Change 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 therapy approaches demonstrate the highest level of efficacy