Chronic Obstructive Pulmonary Disease
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COPD
Evidence-Based Summary and Supporting Research

The Meridian Health COPD evidence review team studied the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2010 updated clinical guidelines for care. The following points of emphasis were derived for clinician use. This summary highlights only those items the review committee deemed important enough to emphasize. Please access the full document for additional information at http://www.goldcopd.org/guidelines-global-strategy-for-diagnosis-management.html.

The four stages of COPD should be used, documented, and communicated consistently across the continuum:
Stage 1: Mild FEV1 ≥ 80% predicted
Stage II: Moderate 50% ≤ FEV1 < 80% predicted
Stage III: Severe 30% ≤ FEV1 < 50% predicted
Stage IV: Very Severe: FEV1 < 30% predictor or FEV1 < 50% predicted plus chronic respiratory failure (All with FEV1/FVC < 0.70)

The modified medical research council dyspnea scale should be performed annually to assess disease progression.

Modified Medical Research Council Dyspnea Scale

Grade

0 “I only get breathless with strenuous exercise”

1 “I get short of breath when hurrying on the level or walking up a slight hill”

2 “I walk slower than people of the same age on the level because of breathlessness or have to stop for breath when walking at my own pace on the level”

3 “I stop for breath after walking about 100 yards or after a few minutes on the level”

4 “I am too breathless to leave the house” or “I am breathless when dressing”
**Spirometry**

- Spirometry assessment is the **gold standard** for diagnosing COPD and monitoring its progression. Quality standards in spirometry measurement must be upheld. For patients with moderate disease or worse, full pulmonary function testing with bronchodilator reversibility testing should be performed. Such testing should also be considered in patients of lower stages whose clinical course is more variable and/or spirometry is not reproducible. Neither bronchodilator nor oral gluco-cortico-steroid reversibility testing predicts disease progression.

A patient’s decline in lung function is best tracked by spirometry measurements, usually no more than once a year.

**In Severe COPD**

- An echocardiogram is recommended.
- ABG measurement while the patient is breathing air is important. Screening less severe cases by pulse oximetry and obtaining ABG if SaO2 is < 92 is reasonable.

**Alpha-1 Antitrypsin Deficiency**

In patients of Caucasian descent who develop COPD at a young age, (< 45 years) or who have a strong family history of the disease, it may be valuable to identify coexisting alpha-1 antitrypsin deficiency.

**Points of Emphasis re: Smoking Cessation**

*Smoking status is critical as this is the single greatest risk factor among U.S. patients.* Clinicians must institutionalize the consistent identification, documentation, and treatment of every tobacco user at every visit. ASK; ADVISE; ASSESS; ASSIST; ARRANGE. Use these 5A’s (see attached algorithm from *Treating Tobacco Use and Dependence: 2008 Update. Quick Reference Guide for Clinicians*).

**Ask every visit.**

Even a brief (3 minute) period of counseling to urge a smoker to quit may result in smoking cessation rates of 5-10%. Practitioners should instruct patients that it may require multiple attempts to be successful.

The quick reference clinician guide may be obtained from [www.ahrq.gov/clinic/tobacco/tobaqr.pdf](http://www.ahrq.gov/clinic/tobacco/tobaqr.pdf).

Combination therapy/strategies for smoking cessation are recommended.

Smith, S. S., et al. (2009). Comparative effectiveness of 5 smoking cessation pharmacotherapies in primary care clinics, Archives of Internal Medicine, 169(22), 2148-2155.

Strongly suggested for clinician review are excerpts enclosed:
- AAFP Pharmacologic Product Guide from the ASK and ACT tobacco cessation program.

**Air Quality**

Persons with advanced COPD should monitor air quality announcements and adjust accordingly.

**Sleep Apnea**

Decision tools for sleep apnea assessments should be used. Use of the STOP BANG screening tool (enclosed) is recommended as it has high sensitivity and specificity.


**Anxiety and Depression**

Anxiety and depression screening is critical. COPD patients may experience 10x the depression as non-COPD patients (NCQA) NCQA. (2009). Insights for improvement: Advancing COPD care through quality measurement.

**Nutrition/Weight Loss or Gain**

Both underweight and overweight are a problem.
A reduction in BMI is an independent risk factor for mortality in COPD (Level A). Advanced COPD patients commonly experience weight loss and this is prognostically important.

**Immunizations**

Influenza and pneumococcal vaccination are strongly recommended.

Influenza vaccines can reduce serious illness and death in COPD by about 50% (Level A).

Pneumococcal polysaccharide vaccine is recommended for COPD patients 65 years and older and has been shown to reduce Community Acquired Pneumonia (CAP) in COPD patients under 65 with FEV1 < 40% predicted (Level B).

**Medications**

*Pharmacologic management per stage* is recommended. See enclosed flow diagram.

**Bronchodilators**

Regular treatment with **long-acting bronchodilators** is more effective and convenient than short acting (Level A).

Oral therapy is slower in onset and has more side effects than inhaled treatment (Level A). Inhaled products, which are absorbed quicker and possess less enduring side effects, are preferred.

Bronchodilator effects of short acting **anticholinergics** last 8 hours and Tiotropium has a duration of more than 24 hours (Level A). Tiotropium (Spiriva) is preferred.

**Methylxanthines:** Toxicity is dose related, with the therapeutic ratio small and most of the benefit occurs only when near-toxic doses are given (Level A).
**Glucocorticosteroids**

Regular treatment with inhaled glucocorticosteroids has been shown to reduce the frequency of exacerbations and thus improve health status for symptomatic COPD patients at stage III and IV and repeated exacerbations (for example, three in the last three years) (Level A).

An inhaled glucocorticosteroid combined with a long acting β2 agonist is more effective than the individual components in reducing exacerbations and improving lung function and health status (Level A).

**Phosphodiesterase-4 Inhibitors (Roflumilast)**

This drug is very recently approved for use in the U.S. and has little track record; its role cannot yet be recommended by local experts. Side effects reported have included weight loss, unexpected diarrhea, behavioral disturbances and depression.

The widespread use of mucolytic agents cannot be recommended at present (Level D).

**Beta Blockers**

Erdman, E. (2009). Safety and tolerability of beta-blockers: Prejudices and reality. *European Heart Journal Supplements, 11*(Supplement A), A21-A25 was reviewed and the following key points of emphasis are significant:

- The majority of patients with HF and COPD can safely tolerate beta-blocker therapy.
- Lung function should be carefully monitored as asthma and COPD may co-exist.
- Especially in elderly, “start low and go slow.”
- Beta-1 selective therapy is preferred.

**Oxygen**

- Long term oxygen therapy is introduced in Stage IV with PaO2 55 mm Hg or SaO2 at/below 88% (Level B). Burden vs. benefit should be assessed. Clinical judgment plays a significant role.
Miscellaneous Key Points

Missed days of work should be assessed each visit.
Reminder: Regular production of sputum for 3 or more months in 2 consecutive years may signal chronic bronchitis.

The presence of wheezing during quiet breathing is a useful pointer to airflow limitation. Wheezing heard only after forced expiration has not been validated as a diagnostic test for COPD.

Less prevalent today in the U.S., but still important for initial and annual assessment, is the presence of occupational or environmental contributors to COPD.

Determine if the patient can financially cover the costs of their prescriptions/therapies.

Routine CT and V-P scanning are appropriate only if the patient is going to surgery.

Exacerbations

• There is no current evidence that the use of antibiotics other than for treating infectious exacerbations of COPD and other bacterial infections is helpful (Level A).
• In the presence of the 3 cardinal signs/indicators, antibiotics of choice are:
  o Azithromycin 500 mg p.o. daily for 5 days. If on amiodarone therapy, may use one of the following:
    ▪ Bactrim DS 1 tab p.o., twice daily x 7 days
    ▪ Amoxicillin 250mg p.o., three times daily x 7 days
    ▪ Doxycycline 100mg p.o., twice daily x 7 days

(Three cardinal signs: increased dyspnea, increased sputum volume, and increased sputum purulence (Level B). The frequency of infections must be assessed.)

Areas of emphasis in exacerbations include:
  o Spirometry and PEF are not accurate during an exacerbation.
  o Pulse oximetry can be used to evaluate oxygen saturation and the need for supplemental oxygen therapy.
  o Home management of COPD exacerbations involves increasing the dose and/or frequency of existing short acting bronchodilator therapy, preferable with a beta-2 agonist (Level A).
Systemic glucocorticosteroids are beneficial in shortening recovery time, improving lung function and hypoxemia (Level A).

**Indications for Hospital Admission Include:**
- Marked increase in intensity of symptoms such as sudden development of resting dyspnea
- Severe underlying COPD
- Onset of new physical signs such as cyanosis, peripheral edema
- Failure of exacerbation to respond to initial medical management
- Significant comorbidities
- Frequent exacerbations
- Newly occurring arrhythmias
- Diagnostic uncertainty
- Older age
- Insufficient home support

**Pulmonologist Consultation**
Signals for referral to the pulmonologist include but are not limited to:
- When long term oral steroid use is being entertained
- Management of alpha 1 antitrypsin deficiency
- Advanced disease where opioids are needed
- NIPPV use
- Surgical management

**Rehabilitation**
- COPD at all stages of disease appears to benefit from exercise training programs, improving both exercise tolerance and symptoms of dyspnea and fatigue (Level A).
- Any patient with COPD should be considered for pulmonary rehab. Use of formal rehab services should be encouraged. Where this is not feasible, home exercise should be encouraged.
- After rehab, guidelines state “if exercise is continued at home the patient’s health status remains above pre rehab levels (Level B).” Nevertheless, the committee noted that attending formal rehab/exercise services does appear to produce social camaraderie and support that promotes adherence.
Benefits of Pulmonary Rehab

1. A program of exercise training of the muscles of ambulation is recommended as a mandatory component of pulmonary rehabilitation for patients with chronic obstructive pulmonary disease (COPD). **Grade of Recommendation 1A**
2. Pulmonary rehabilitation improves the symptom of dyspnea in patients with COPD. **Grade of Recommendation 1A**
3. Pulmonary rehabilitation improves health related quality of life (HRQOL) in patients with COPD. **Grade of Recommendation 1A**
4. Pulmonary rehabilitation reduces the number of hospital days and other measures of health-care utilization in patients with COPD. **Grade of Recommendation 2B**
5. Pulmonary rehabilitation is cost-effective in patients with COPD. **Grade of Recommendation 2C**


Disease Management Review

The committee reviewed the evidence (SR) from Lemmens (2008) and the more recent large VA Study by Rice (2010). The committee concurred that there should be an emphasis for the system practitioners in the following:

- Provider education
- Patient education/self management
- Case management across the continuum

This triple combination has been showed in meta-analysis to reduce the chance of ≥ 1 hospitalization as well as improve quality of life. The VA study strongly pointed to a reduction of hospitalizations and ER visits with disease management (DM). As Meridian evolves their COPD DM Services in provider education, patient education and case management, their use should be encouraged.


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Levels of Evidence Used in the GOLD Guidelines

A Randomized controlled trials with rich body of data.
B Randomized controlled trials with limited body of data.
C Nonrandomized trials; observational studies.
D Panel consensus judgment.

Table 1. Stepwise Pharmacologic Therapy in COPD

<table>
<thead>
<tr>
<th>Stage</th>
<th>Spirometry Findings</th>
<th>Recommended Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I: mild COPD</td>
<td>$FEV_1/FVC &lt; 70%; \quad FEV_1 \geq 80%$</td>
<td><strong>Prescribe</strong> a short-acting bronchodilator to be used as needed: anticholinergic (ipratropium) or beta$_2$-agonist (albuterol, levalbuterol, terbutaline)</td>
</tr>
<tr>
<td>Stage II: moderate COPD</td>
<td>$FEV_1/FVC &lt; 70%; \quad 50% \leq FEV_1 &lt; 80%$</td>
<td><strong>Add</strong> one or more long-acting bronchodilators on a scheduled basis: long-acting anticholinergic (tiotropium) or long-acting beta$_2$-agonist (salmeterol, formoterol, R-R formoterol)  <strong>Consider</strong> referring for pulmonary rehabilitation</td>
</tr>
<tr>
<td>Stage III: severe COPD</td>
<td>$FEV_1/FVC &lt; 70%; \quad 30% \leq FEV_1 &lt; 50%$</td>
<td><strong>Add</strong> inhaled corticosteroid (beclomethasone, budesonide, flunisolide, fluticasone, triamcinolone; or combination salmeterol/fluticasone) if patient has repeated exacerbations</td>
</tr>
<tr>
<td>Stage IV: very severe COPD</td>
<td>$FEV_1/FVC &lt; 70%; \quad FEV_1 &lt; 30%$</td>
<td><strong>Evaluate</strong> need for supplemental oxygen therapy  <strong>Consider</strong> surgical options</td>
</tr>
</tbody>
</table>

*Abbreviation: COPD, chronic obstructive pulmonary disease; FEV$_1$, forced expiratory volume in 1 second; FVC, forced vital capacity.*

Source: University of Pennsylvania, accessed from the page Penn CME/Best Practice  
http://penncmebestpractice.org/category/references/resource?page=1
STOP BANG Screening for Obstructive Sleep Apnea

Answer the following questions to find out if you are at risk for Obstructive Sleep Apnea:

**STOP**

S (snore)       Have you been told that you snore? YES/NO
T (tired)       Are you often tired during the day? YES/NO
O (obstruction) Do you know if you stop breathing or has anyone witnessed you stop breathing while you are asleep? YES/NO
P (pressure)    Do you have high blood pressure or on medication to control high blood pressure? YES/NO

If you answered YES to two or more questions on the STOP portion you are at risk for Obstructive Sleep Apnea. It is recommended that you contact your primary care provider to discuss a possible sleep disorder.

To find out if you are at moderate to severe risk of Obstructive Sleep Apnea, complete the BANG questions below.

**BANG**

B (BMI)       Is your body mass index greater than $30$? YES/NO
A (age)       Are you $50$ years old or older? YES/NO
N (neck)      Do you have a neck circumference greater than $40$ cm? YES/NO
G (gender)    Are you a male? YES/NO

The more questions you answer YES to on the BANG portion, the greater your risk of having moderate to severe Obstructive Sleep Apnea.


<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Tobacco dependence is a chronic disease that often requires repeated intervention and multiple attempts to quit. Effective treatments exist, however, that can significantly increase rates of long-term abstinence.</td>
</tr>
<tr>
<td>2</td>
<td>It is essential that clinicians and health care delivery systems consistently identify and document tobacco use status and treat every tobacco user seen in a health care setting.</td>
</tr>
<tr>
<td>3</td>
<td>Tobacco dependence treatments are effective across a broad range of populations. Clinicians should encourage every patient willing to make a quit attempt to use the counseling treatments and medications recommended in this guideline.</td>
</tr>
<tr>
<td>4</td>
<td>Brief tobacco dependence treatment is effective. Clinicians should offer every patient who uses tobacco at least the brief treatments shown to be effective in this guideline.</td>
</tr>
<tr>
<td>5</td>
<td>Individual, group, and telephone counseling are effective, and their effectiveness increases with treatment intensity. Two components of counseling are especially effective, and clinicians should use these when counseling patients making a quit attempt: (a) practical counseling (problem-solving/skills training) and (b) social support delivered as part of treatment.</td>
</tr>
<tr>
<td>6</td>
<td>Numerous effective medications are available for tobacco dependence, and clinicians should encourage their use by all patients attempting to quit smoking—except where medically contraindicated or with specific populations for which there is insufficient evidence of effectiveness (i.e., pregnant women, smokeless tobacco users, light smokers, and adolescents). Seven first-line medications (5 nicotine and 2 non-nicotine) reliably increase long-term smoking abstinence rates: bupropion SR, nicotine gum, nicotine inhaler, nicotine lozenge, nicotine nasal spray, nicotine patch, and varenicline. Clinicians also should consider the use of certain combinations of medications identified as effective in this guideline.</td>
</tr>
<tr>
<td>7</td>
<td>Counseling and medication are effective when used by themselves for treating tobacco dependence. The combination of counseling and medication, however, is more effective than either alone. Thus, clinicians should encourage all individuals making a quit attempt to use both counseling and medication.</td>
</tr>
<tr>
<td>8</td>
<td>Telephone quitline counseling is effective with diverse populations and has broad reach. Therefore, both clinicians and health care delivery systems should ensure patient access to quitlines and promote quitline use.</td>
</tr>
<tr>
<td>9</td>
<td>If a tobacco user currently is unwilling to make a quit attempt, clinicians should use the motivational treatments shown in this guideline to be effective in increasing future quit attempts.</td>
</tr>
<tr>
<td>10</td>
<td>Tobacco dependence treatments are both clinically effective and highly cost-effective relative to interventions for other clinical disorders. Providing coverage for these treatments increases quit rates. Insurers and purchasers should ensure that all insurance plans include the counseling and medication identified as effective in this guideline and covered benefits.</td>
</tr>
</tbody>
</table>

Figure 1. The “5 A’s”: Treating Tobacco Dependence as a Chronic Disease

From the quick reference guide found at:
### Nicotine Replacement Therapy (NRT) Formulations

<table>
<thead>
<tr>
<th>Gum</th>
<th>Lozenge</th>
<th>Transdermal Patch</th>
<th>Nasal Spray</th>
<th>Oral Inhaler</th>
<th>Bupropion SR</th>
<th>Varenicline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicorette1, Generic</td>
<td>Nicorette Lozenge1</td>
<td>Nicoderm CQ, Generic</td>
<td>Nicotrol NSP</td>
<td>Nicotrol Inhaler2</td>
<td>Zyban1, Generic</td>
<td>Chantix2</td>
</tr>
<tr>
<td>2 mg, 4 mg</td>
<td>Original, cinnamon, fruit, mint, orange</td>
<td>OTC (Nicoderm CQ, generic)</td>
<td>Rx (generic)</td>
<td>Rx</td>
<td>Rx</td>
<td>Rx</td>
</tr>
</tbody>
</table>

#### Bupropion SR

- **Contraindications**: Concomitant therapy with medications or medical conditions known to lower the seizure threshold
- **Warnings**: Severe renal impairment (dosage adjustment is necessary)
  - Pregnancy (category C) and breastfeeding
  - Adolescents (<18 years)

#### Varenicline

- **Warnings**: Black-boxed warning for neuropsychiatric symptoms
  - Cardiovascular adverse events in patients with existing cardiovascular disease

### Precautions

- **Recent (<2 weeks) myocardial infarction**
- **Serious underlying arrhythmias**
- **Recent (<2 weeks) myocardial infarction**
- **Serious underlying arrhythmias**
- **Serious or worsening angina pectoris**
- **Adolescents (<18 years)**

### Dosing

**1st cigarette ≤30 minutes after waking**

- **Gum**: 2 mg
- **Lozenge**: 4 mg
- **Transdermal Patch**: 7 mg
- **Nasal Spray**: 0.5 mg/cartridge
- **Oral Inhaler**: 0.5 mg
- **Bupropion SR**: 150 mg/day
- **Varenicline**: 0.5 mg/day

**1st cigarette >30 minutes after waking**

- **Gum**: 4 mg
- **Lozenge**: 7 mg
- **Transdermal Patch**: 14 mg
- **Nasal Spray**: 0.5 mg
- **Oral Inhaler**: 0.5 mg
- **Bupropion SR**: 150 mg/day
- **Varenicline**: 0.5 mg/day

**Weeks 1–6**

- **Gum**: 1 piece q 1–2 hours
- **Lozenge**: 1 lozenge q 1–2 hours
- **Transdermal Patch**: 1 cartridge q 1–2 hours
- **Nasal Spray**: 1–2 doses/hour
- **Oral Inhaler**: Individualizing dosing
- **Bupropion SR**: 100 mg/day
- **Varenicline**: 0.5 mg/day

**Weeks 7–9**

- **Gum**: 1 piece q 2–4 times/day
- **Lozenge**: 1 lozenge q 2–4 hours
- **Transdermal Patch**: 1 lozenge q 4–8 hours
- **Nasal Spray**: May wear patch for 16 hours if patient experiences sleep disturbances (remove at bedtime)
- **Oral Inhaler**: Duration: 8–10 weeks
- **Bupropion SR**: 150 mg/day
- **Varenicline**: 0.5 mg/day

**Weeks 10–12**

- **Gum**: Maximum, 24 pieces/day
- **Lozenge**: Chew each piece slowly
- **Transdermal Patch**: Park between cheek and gum when peppy or tingling sensation appears (~15–30 chews)
- **Nasal Spray**: Repeat chew/park steps until most of the nicotine is gone (tongue does not return; generally 30 min)
- **Oral Inhaler**: Duration: up to 12 weeks
- **Bupropion SR**: Days 1–3: 0.5 mg po AM x 3 days, then 150 mg po bid
- **Varenicline**: Days 1–3: 0.5 mg po AM

**Adolescents (<18 years)**

- **Gum**: 2 mg
- **Lozenge**: 4 mg
- **Transdermal Patch**: 7 mg
- **Nasal Spray**: 0.5 mg
- **Oral Inhaler**: 0.5 mg
- **Bupropion SR**: 75 mg/day
- **Varenicline**: 0.3 mg/day

**Duration**

- **Gum**: 6–16 cartridges/day
- **Lozenge**: 1–2 doses/hour
- **Transdermal Patch**: ≤70 cigarettes/day
- **Nasal Spray**: 1–2 doses/hour
- **Oral Inhaler**: 1–2 doses/hour
- **Bupropion SR**: ≥150 mg/day
- **Varenicline**: ≤150 mg/day

**Days 1–3**

- **Gum**: 0.5 mg po AM x 3 days, then 150 mg po bid
- **Lozenge**: 150 mg/day
- **Transdermal Patch**: 150 mg/day
- **Nasal Spray**: 150 mg/day
- **Oral Inhaler**: 150 mg/day
- **Bupropion SR**: 150 mg/day
- **Varenicline**: 150 mg/day

**Duration**

- **Gum**: 6–16 cartridges/day
- **Lozenge**: 1–2 doses/hour
- **Transdermal Patch**: ≤70 cigarettes/day
- **Nasal Spray**: 1–2 doses/hour
- **Oral Inhaler**: 1–2 doses/hour
- **Bupropion SR**: ≥150 mg/day
- **Varenicline**: ≤150 mg/day

**Side Effects**

- **Gum**: Frequent: Jaw pain, dry mouth
- **Lozenge**: Frequent: Jaw pain, dry mouth
- **Transdermal Patch**: Frequent: Skin rash, itching
- **Nasal Spray**: Frequent: Runny nose, sneezing
- **Oral Inhaler**: Frequent: Dry mouth, throat irritation
- **Bupropion SR**: Frequent: Dry mouth, constipation
- **Varenicline**: Frequent: Dry mouth, constipation
# Nicotine Replacement Therapy (NRT) Formulations

## Adverse Effects

<table>
<thead>
<tr>
<th>Gum</th>
<th>Lozenge</th>
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<th>Bupropion SR</th>
<th>Varenicline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouth/jaw soreness</td>
<td>Nausea</td>
<td>Local skin reactions (erythema, pruritus, burning)</td>
<td>Nasal and/or throat irritation (hot, peppery, or burning sensation)</td>
<td>Mouth and/or throat irritation</td>
<td>Insomnia</td>
<td>Nausea</td>
</tr>
<tr>
<td>Hiccups</td>
<td>Hiccups</td>
<td>Headache</td>
<td>Cough</td>
<td>Cough</td>
<td>Dry mouth</td>
<td>Sleep disturbances (insomnia, abnormal/vivid dreams)</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>Cough</td>
<td>Sleep disturbances (insomnia, abnormal/vivid dreams); associated with nocturnal nicotine absorption</td>
<td>Headache</td>
<td>Headache</td>
<td>Nasal congestion</td>
<td>Constipation</td>
</tr>
<tr>
<td>Hypersalivation</td>
<td>Heartburn</td>
<td>Headache</td>
<td>Headache</td>
<td>Headache</td>
<td>Rash</td>
<td>Flatulence</td>
</tr>
<tr>
<td>Effects associated with incorrect chewing technique: - Lightheadedness</td>
<td>Nausea</td>
<td>Flatulence</td>
<td>Nervousness/difficulty concentrating</td>
<td>Hiccups</td>
<td>Constipation</td>
<td>Vomiting</td>
</tr>
<tr>
<td>- Nausea/vomiting</td>
<td>Urination</td>
<td>Insomnia</td>
<td>Insomnia</td>
<td>Hiccups</td>
<td>Seizures (risk is 0.1%)</td>
<td>Neuropsychiatric symptoms (rare; see PRECAUTIONS)</td>
</tr>
<tr>
<td>- Throat and mouth irritation</td>
<td>Rhinitis</td>
<td>Hyposalivation</td>
<td>Constipation</td>
<td>Rash</td>
<td>Neurologic symptoms (rare; see PRECAUTIONS)</td>
<td></td>
</tr>
</tbody>
</table>

## Advantages

<table>
<thead>
<tr>
<th>Gum</th>
<th>Lozenge</th>
<th>Transdermal Patch</th>
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<th>Varenicline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Might satisfy oral cravings</td>
<td>Might satisfy oral cravings</td>
<td>Provides consistent nicotine levels over 24 hours</td>
<td>Patients can initiate therapy to rapidly manage withdrawal symptoms</td>
<td>Patients can titrate therapy to manage withdrawal symptoms</td>
<td>Easy to use; oral formulation might be associated with fewer compliance problems</td>
<td>Easy to use; oral formulation might be associated with fewer compliance problems</td>
</tr>
<tr>
<td>Might delay weight gain</td>
<td>Might delay weight gain</td>
<td>Easy to use and conceal</td>
<td>Patients can titrate therapy to manage withdrawal symptoms</td>
<td>Patients can titrate therapy to manage withdrawal symptoms</td>
<td>Can be used with NRT</td>
<td>Offers a new mechanism of action for patients who have failed other agents</td>
</tr>
<tr>
<td>Patients can titrate therapy to manage withdrawal symptoms</td>
<td>Patients can titrate therapy to manage withdrawal symptoms</td>
<td>Once daily dosing associated with fewer compliance problems</td>
<td>Patients can titrate therapy to manage withdrawal symptoms</td>
<td>Patients can titrate therapy to manage withdrawal symptoms</td>
<td>Might be beneficial in patients with depression</td>
<td></td>
</tr>
<tr>
<td>Variety of flavors are available</td>
<td>Variety of flavors are available</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

## Disadvantages

<table>
<thead>
<tr>
<th>Gum</th>
<th>Lozenge</th>
<th>Transdermal Patch</th>
<th>Nasal Spray</th>
<th>Oral Inhaler</th>
<th>Bupropion SR</th>
<th>Varenicline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Need for frequent dosing can compromise compliance</td>
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<td>Patients cannot titrate the dose to acutely manage withdrawal symptoms</td>
<td>Need for frequent dosing can compromise compliance</td>
<td>Need for frequent dosing can compromise compliance</td>
<td>Seizure risk is increased</td>
<td>May induce nausea in up to one third of patients</td>
</tr>
<tr>
<td>Might be problematic for patients with significant dental work</td>
<td>Gastrointestinal side effects (nausea, hiccups, heartburn) might be bothersome</td>
<td>Allergic reactions to adhesive might occur</td>
<td>Nasal/throat irritation may be bothersome</td>
<td>Initial throat or mouth irritation can be bothersome</td>
<td>Several contraindications and precautions preclude use in some patients (see PRECAUTIONS)</td>
<td></td>
</tr>
<tr>
<td>Patients must use proper chewing technique to minimize adverse effects</td>
<td>Patients with dermatologic conditions should not use the patch</td>
<td>Patients with dermatologic conditions should not use the patch</td>
<td>Patients with bronchospastic disease should not use the spray</td>
<td>Cartridges should not be stored in very warm conditions or used in very cold conditions</td>
<td>Patients should be monitored for potential neuropsychiatric symptoms (rare; see PRECAUTIONS)</td>
<td></td>
</tr>
<tr>
<td>Gum chewing may not be socially acceptable</td>
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</tbody>
</table>

## Cost/Day

<table>
<thead>
<tr>
<th>Gum</th>
<th>Lozenge</th>
<th>Transdermal Patch</th>
<th>Nasal Spray</th>
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</tr>
</thead>
<tbody>
<tr>
<td>2 mg or 4 mg: $1.90–$5.49 (9 pieces)</td>
<td>2 mg or 4 mg: $1.89–$4.50 (9 pieces)</td>
<td>$1.60–$3.40 (1 patch)</td>
<td>$3.58 (8 doses)</td>
<td>$6.39 (6 cartridges)</td>
<td>$2.71–$6.20 (2 tablets)</td>
<td>$5.64–$5.96 (2 tablets)</td>
</tr>
</tbody>
</table>

1 Marketed by GlaxoSmithKline.
2 Marketed by Pfizer.
3 The U.S. Clinical Practice Guideline states that pregnant smokers should be encouraged to quit without medication based on insufficient evidence of effectiveness and theoretical concerns with safety. Pregnant smokers should be offered behavioral counseling interventions that exceed minimal advice to quit.
4 In July 2009, the FDA mandated that the prescribing information for all bupropion- and varenicline-containing products include a black-boxed warning highlighting the risk of serious neuropsychiatric symptoms, including changes in behavior, hostility, agitation, depressed mood, suicidal thoughts and behavior, and attempted suicide. Clinicians should advise patients to stop taking varenicline or bupropion SR and contact a healthcare provider immediately if they experience agitation, depressed mood, and any changes in behavior that are not typical of nicotine withdrawal, or if they experience suicidal thoughts or behavior. If treatment is stopped due to neuropsychiatric symptoms, patients should be monitored until the symptoms resolve.
5 Wholesale acquisition cost from Red Book Online. Thomson Reuters, March 2012.

Abbreviations: MAO, monoamine oxidase; NRT, nicotine replacement therapy; OTC, over-the-counter (non-prescription product); Rx, prescription product.

For complete prescribing information, please refer to the manufacturers' package inserts.

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