<table>
<thead>
<tr>
<th>NICOTINE REPLACEMENT THERAPY (NRT) FORMULATIONS</th>
<th>BUPROPION SR</th>
<th>VARENICLINE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GUM</strong></td>
<td>Nicorette¹, Generic Nicorette², Generic Nicorette³ mini OTC</td>
<td>Nicorette, Generic Nicorette³ mini OTC</td>
</tr>
<tr>
<td><strong>LOZENGE</strong></td>
<td>Habitrol®, NicoDerm CO¹, Generic OTC</td>
<td>Nicorette NS¹</td>
</tr>
<tr>
<td><strong>TRANSDERMAL PATCH</strong></td>
<td>Nicorette, Generic Nicorette³ mini OTC</td>
<td>Nicorette NS¹</td>
</tr>
<tr>
<td><strong>NASAL SPRAY</strong></td>
<td>7 mg, 14 mg, 21 mg (24-hr release)</td>
<td>Nicorette NS¹</td>
</tr>
<tr>
<td><strong>ORAL INHALER</strong></td>
<td>10 mg/mL nicotine solution</td>
<td>Nicorette Inhaler¹</td>
</tr>
<tr>
<td><strong>BUPROPION SR</strong></td>
<td>Rx</td>
<td>Nicorette Inhaler¹</td>
</tr>
<tr>
<td><strong>VARENICLINE</strong></td>
<td>150 mg sustained-release tablet</td>
<td>Nicorette Inhaler¹</td>
</tr>
</tbody>
</table>

**PRECAUTIONS**

- Recent (≤2 weeks) myocardial infarction
- Serious underlying arrhythmias
- Serious or worsening angina pectoris
- Temporomandibular joint disease
- Pregnancy and breastfeeding
- Adolescents (<18 years)
- Recent (≤2 weeks) myocardial infarction
- Serious underlying arrhythmias
- Serious or worsening angina pectoris
- Pregnancy and breastfeeding
- Adolescents (<18 years)
- Recent (≤2 weeks) myocardial infarction
- Serious underlying arrhythmias
- Serious or worsening angina pectoris
- Underlying chronic nasal disorders (rhinitis, nasal polyps, sinusitis)
- Severe reactive airway disease
- Pregnancy and breastfeeding
- Adolescents (<18 years)
- Concomitant therapy with medications/conditions known to lower the seizure threshold
- Hepatic impairment
- Pregnancy and breastfeeding
- Adolescents (<18 years)
- Treatment-emergent neuropsychiatric symptoms

**Contraindications:**
- Seizure disorder
- Concomitant bupropion (e.g., Wellbutrin) therapy
- Current or prior diagnosis of bulimia or anorexia nervosa
- Simultaneous abrupt discontinuation of alcohol or sedatives/benzodiazepines
- MAO inhibitors in preceding 14 days; concurrent use of reversible MAO inhibitors

**DOSING**

- 1st cigarette ≤30 minutes after waking: 4 mg
- 1st cigarette >30 minutes after waking: 2 mg
- Weeks 1–6:
  - 1 piece q 1–2 hours
  - 1 piece q 2–4 hours
  - Weeks 7–9:
  - 1 piece q 4–8 hours
- While awake
- Maximum, 24 pieces/day
- During initial 6 weeks of treatment, use at least 9 pieces/day
- Chew each piece slowly
- Park between cheek and gum when peppery or tingling sensation appears (~15–30 chews)
- Resume chewing when tingle fades
- Repeat chew/park steps until most of the nicotine is gone (tingle does not return; generally 30 min)
- Park in different areas of mouth
- No food or beverages 15 minutes before or during use
- Duration: up to 12 weeks

- 1st cigarette ≤30 minutes after waking: 4 mg
- 1st cigarette >30 minutes after waking: 2 mg
- Weeks 1–6:
  - 1 lozenge q 1–2 hours
  - 1 lozenge q 2–4 hours
  - 1 lozenge q 4–8 hours
- While awake
- Maximum, 20 lozenges/day
- During initial 6 weeks of treatment, use at least 9 lozenges/day
- Allow to dissolve slowly (20–30 minutes)
- Nicotine release may cause a warm, tingling sensation
- Do not chew or swallow
- Occasionally rotate to different areas of the mouth
- No food or beverages 15 minutes before or during use
- Duration: up to 12 weeks

- >10 cigarettes/day:
  - 21 mg/day x 4–6 weeks
  - 14 mg/day x 2 weeks
  - 7 mg/day x 2 weeks
- ≤10 cigarettes/day:
  - 14 mg/day x 6 weeks
  - 7 mg/day x 2 weeks
- Rotate patch application site daily; do not apply a new patch to the same skin site for at least one week
- May wear patch for 16 hours if patient experiences sleep disturbances (remove at bedtime); before recommending, rule out other factors that might be contributing (e.g., drug interaction between caffeine and tobacco smoke, other medications, and lifestyle factors)
- Duration: 6–10 weeks

- 1–2 doses/hour
  - (6–40 doses/day)
- One dose = 2 sprays (one in each nostril); each spray delivers 0.5 mg of nicotine to the nasal mucosa
- While awake
- Maximum
  - 5 doses/hour or
  - 40 doses/day
- During initial 6–8 weeks of treatment, use at least 9 doses/day
- Gradually reduce daily dosage over an additional 4–6 weeks
- Do not sniff, swallow, or inhale through the nose as the spray is being administered
- Duration: 12 weeks

- 6–16 cartridges/day
- Individualize dosing; initially use 1 cartridge q 1–2 hours
  - While awake
- Best effects with continuous puffing for 20 minutes
- During initial 6 weeks of treatment use at least 6 cartridges/day
- Gradually reduce daily dosage over the following 6–12 weeks
- Nicotine in cartridge is depleted after 20 minutes of active puffing
- Inhale into back of throat or puff in short breaths
- Do NOT inhale into the lungs (like a cigarette) but “puff” as if lighting a pipe
- Open cartridge retains potency for 24 hours
- No food or beverages 15 minutes before or during use
- Duration: 3–6 months

150 mg po q AM x 3 days, then 150 mg po bid
- Do not exceed 300 mg/day
- Begin therapy 1–2 weeks prior to quit date
- Allow at least 8 hours between doses
- Avoid bedtime dosing to minimize insomnia
- Dose tapering is not necessary
- Duration: 7–12 weeks, with maintenance up to 6 months in selected patients

Days 1–3: 0.5 mg po AM
Days 4–7: 0.5 mg po bid
Weeks 2–12: 1 mg po bid
- Begin therapy 1 week prior to quit date
- Take dose after eating and with a full glass of water
- Dose tapering is not necessary
- Dosing adjustment is necessary for patients with severe renal impairment
- Duration: 12 weeks; an additional 12-week course may be used in selected patients
- May initiate up to 35 days before target quit date OR may reduce smoking over a 12-week period of treatment prior to quitting and continue treatment for an additional 12 weeks
<table>
<thead>
<tr>
<th>NICOTINE REPLACEMENT THERAPY (NRT) FORMULATIONS</th>
<th>BUPROPION SR</th>
<th>VARENICLINE</th>
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</thead>
<tbody>
<tr>
<td><strong>GUM</strong></td>
<td>Mouth and throat irritation</td>
<td>Insomnia</td>
</tr>
<tr>
<td>Jaw muscle soreness</td>
<td>Mouth and throat irritation</td>
<td>Dry mouth</td>
</tr>
<tr>
<td>Hiccup</td>
<td>Hiccup</td>
<td>Nausea</td>
</tr>
<tr>
<td>GI complaints (dyspepsia, nausea)</td>
<td>GI complaints (dyspepsia, nausea)</td>
<td>Anxiety/difficulty concentrating</td>
</tr>
<tr>
<td><strong>ADVERSE EFFECTS</strong></td>
<td>Might serve as an oral substitute for tobacco</td>
<td>Seizures (risk is 0.15%)</td>
</tr>
<tr>
<td>Might delay weight gain</td>
<td>Might delay weight gain</td>
<td>Neuropsychiatric symptoms (rare; see PRECAUTIONS)</td>
</tr>
<tr>
<td>Can be titrated to manage withdrawal symptoms</td>
<td>Can be titrated to manage withdrawal symptoms</td>
<td></td>
</tr>
<tr>
<td>Can be used in combination with other agents to manage situational urges</td>
<td>Can be used in combination with other agents to manage situational urges</td>
<td></td>
</tr>
<tr>
<td>Relatively inexpensive</td>
<td>Relatively inexpensive</td>
<td></td>
</tr>
<tr>
<td><strong>ADVANTAGES</strong></td>
<td>Need for frequent dosing can compromise adherence</td>
<td>Twin daily oral dosing is simple and associated with fewer adherence problems</td>
</tr>
<tr>
<td>Might be problematic for patients with significant dental work</td>
<td>Might be problematic for patients with significant dental work</td>
<td>Offers a different mechanism of action for patients who have failed other agents</td>
</tr>
<tr>
<td>Proper chewing technique is necessary for effectiveness and to minimize adverse effects</td>
<td>Proper chewing technique is necessary for effectiveness and to minimize adverse effects</td>
<td>Most effective cessation agent when used as monotherapy</td>
</tr>
<tr>
<td>Gum chewing might not be acceptable or desirable for some patients</td>
<td>Gum chewing might not be acceptable or desirable for some patients</td>
<td></td>
</tr>
<tr>
<td><strong>DISADVANTAGES</strong></td>
<td>Need for frequent dosing can compromise adherence</td>
<td>Seizure risk is increased</td>
</tr>
<tr>
<td>Need for frequent dosing cannot compromise adherence</td>
<td>Need for frequent dosing cannot compromise adherence</td>
<td>Several contraindications and precautions preclude use in some patients (see PRECAUTIONS)</td>
</tr>
<tr>
<td>Gastrointestinal side effects (nausea, hiccup, heartburn) might be bothersome</td>
<td>Gastrointestinal side effects (nausea, hiccup, heartburn) might be bothersome</td>
<td>Patients should be monitored for potential neuropsychiatric symptoms (see PRECAUTIONS)</td>
</tr>
<tr>
<td>When used as monotherapy, cannot be titrated to acutely manage withdrawal symptoms</td>
<td>When used as monotherapy, cannot be titrated to acutely manage withdrawal symptoms</td>
<td>Cost of treatment</td>
</tr>
<tr>
<td>Not recommended for use by patients with dermatologic conditions (e.g., psoriasis, eczema, atopic dermatitis)</td>
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<td></td>
</tr>
<tr>
<td><strong>COST</strong></td>
<td>Cost/day</td>
<td>Cost/day</td>
</tr>
<tr>
<td>2 mg or 4 mg: $1.90–$5.48 (9 pieces)</td>
<td>2 mg or 4 mg: $1.99–$4.20 (9 pieces)</td>
<td>2 mg or 4 mg: $1.99–$4.20 (9 pieces)</td>
</tr>
<tr>
<td>$1.52–$3.49 (1 patch)</td>
<td>$10.63 (8 doses)</td>
<td>$18.06 (6 cartridges)</td>
</tr>
<tr>
<td>$17.72 [Chantix]</td>
<td>$13.76 [generic] (2 tablets)</td>
<td></td>
</tr>
</tbody>
</table>

1 Marked by GlaxoSmithKline.
2 Marked by Dr. Reddy’s.
3 Marked by Pfizer.
4 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.
5 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 health care provider immediately if they experience agitation, depressed mood, or 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. Based on results of a mandated clinical trial, the FDA removed this boxed warning in December 2016.
6 Approximate cost based on the recommended initial dosing for each agent and the wholesale acquisition cost from Red Book Online. Thomson Reuters, January 2023.

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

For complete prescribing information and a comprehensive listing of warnings and precautions, please refer to the manufacturers’ package inserts.

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