# NYSMPEP Smoking Cessation Guidance:

# Key Message 3

**Key Message 3**: All smokers trying to quit should be offered medication (except when contraindicated or for specific populations). The Agency for Healthcare Research and Quality (AHRQ) and United States Preventive Services Task Force (USPSTF) recommend nicotine replacement therapy, bupropion sustained-release (SR), or varenicline for first-line treatment of tobacco use.

## First-Line Medications

The nicotine replacement therapies (NRTs) are FDA-approved as aids to smoking cessation through relief of nicotine withdrawal symptoms (including nicotine craving). Nicotine is a parasympathominetic alkaloid. Adverse effects commonly observed with nicotine replacement agents are nausea and vomiting, sleep disturbances, headache, and chest pain. Table 1 compares the effectiveness of currently available smoking cessation pharmacotherapies to placebo. Currently available NRTs are listed in Table 2. Additional first-line medications include non-nicotine pharmacologic agents; bupropion SR (Zyban®) and varenicline (Chantix®) listed in Table 3.

## Combination Therapies

**The combination of 2 NRTs, specifically the transdermal system combined with another NRT dosage form (i.e., gum, lozenge, spray or inhaler), has been shown to be more effective than NRT monotherapy (see Table 1).**[2] Concomitant use of bupropion SR and nicotine transdermal system has also been shown to be efficacious**.** Varenicline in combination with NRT can potentially result in adverse events due to its nicotine antagonist properties**.** Combining behavioral interventions and pharmacotherapy can also improve smoking cessation rates**.**

## Effectiveness of Smoking Cessation Pharmacotherapies (Meta-Analyses and Systematic Reviews)

**Table 1: Effectiveness of Smoking Cessation Pharmacotherapies Compared to Placebo**[1,2]

| | AHRQ | | USPSTF | |
|---|---|---|---|---|
| | Odds Ratio (95% CI) | Abstinence Rate (95% CI) | Relative Risk (95% CI) | Abstinence Rate |
| Placebo | 1.0 | 13.8 | | 10-12% |
| *First-Line Therapies* | | | | |
| Bupropion SR | 2.0 (1.8-2.2) | 24.2 (22.2-26.4) | 1.62 (1.61-2.36) | 19.7% |
| Nicotine gum | 1.5 (1.2-1.7) | 19.0 (16.5-21.9) | 1.49 (1.40-1.60) | 17.3% |
| Nicotine inhaler | 2.1 (1.5-2.9) | 24.8 (19.1-31.6) | | |
| Nicotine lozenge | -- | -- | 1.95 (1.61-2.36) | |
| Nicotine nasal spray | 2.3 (1.7-3.0) | 26.7 (21.5-32.7) | -- | |
| Nicotine patch | 1.9 (1.7-2.2) | 23.4 (21.3-25.8) | 1.64 (1.52-1.78) | |
| Varenicline (2 mg/day) | 3.1 (2.5-3.8) | 33.2 (28.9-37.8) | 2.27 (2.02-2.55) | 28.0% |
| *Combination Therapies* | | | | |
| **Nicotine patch + *as needed* NRT** | **3.6 (2.5-5.2)** | **36.5 (28.6-45.3)** | **1.34 (1.18-1.51)** | **20.6%** |
| Nicotine patch + inhaler | 2.2 (1.3-3.6) | 25.8 (16.1-35.0) | | |
| Nicotine patch + bupropion SR | 2.5 (1.9-3.4) | 28.9 (23.5-35.1) | 1.24 (1.06-1.45) | -- |
| *Second-Line Agents** | | | | |
| Clonidine | 2.1 (1.2-3.7) | 25.0 (15.7-37.3) | -- | -- |
| Nortriptyline | 1.8 (1.3-2.6) | 22.5 (16.8-29.4) | -- | -- |

CI=confidence interval; NRT=nicotine replacement therapy; SR=sustained-release
**AHRQ considers these medications to be second-line options on a case-by-case basis after first-line medication/s have failed. These agents use is only supported by compendia and are NOT FDA-approved to treat tobacco dependence. Use is associate with greater safety concerns.*

Odd ratio (OR) = OR represents the odds that an outcome will occur given a particular exposure, compared to the odds of the outcome occurring in the absence of that exposure

Relative Risk (RR) = RR represents the risk of a certain event happening in one group compared to the risk of the same event happening in another group

| Table 2: Nicotine Replacement Therapies[1-6] | | | | | | |
|---|---|---|---|---|---|---|
| **Products*** | **Availability** | **Dosage** | **Administration** | **Common Side Effects** | **Warnings and Precautions** | **Additional Concerns**** |
| **Gum** | 2 and 4 mg<br><br>Nicorette®, generic | *Based on time to 1st cigarette of day*:<br>>30 min – 2 mg<br><30 min – 4 mg<br><br>*Based on CPD*:<br><25 – 2 mg<br>>25 – 4 mg<br><br>Weeks 1-6: 1 piece every 1-2 h (Use at least 9 pieces of gum /day for the first 6 weeks of therapy to improve success rate)<br><br>Weeks 7-9: 1 piece every 2-4 h<br>Weeks 10-12: 1 piece every 4-8 h<br><br>MDD: 24 pieces<br><br>Duration: 12 weeks | Chew gum slowly until it tingles then park it between check and gum.<br><br>When tingle is gone, repeat.<br><br>Do not eat or drink for 15 minutes before or during chewing.<br><br>Do not swallow. | Mouth soreness, hiccups, dyspepsia, jaw ache | Avoid in patients with dental disease and TMJ<br><br>Use with caution in patients on a sodium-restricted diet (11 mg of sodium/piece of gum) | **Cardiovascular**: Nicotine can increase heart rate and blood pressure; avoid use during immediate post-myocardial infarction period, in serious arrhythmias, or severe angina<br><br>**Gastrointestinal**: Nicotine can delay healing of active peptic ulcer disease<br><br>**Use during pregnancy**: Evidence on the benefits of these therapies to achieve tobacco cessation in pregnant women is inadequate, and the benefits-to-harms ratio cannot be determined. |
| **Inhaler** | 10 mg/cartridge delivering 4 mg of nicotine<br><br>Nicotrol® Inhaler | 6 to 16 cartridges (24 to 64 mg) per day for up to 12 wks, followed by gradual taper over 6-12 wks<br><br>MDD: 16 cartridges<br><br>Duration: 6 months | Best effect achieved by frequent continuous puffing (20 minutes). | Local irritation, cough, rhinitis, dyspepsia, headache | Use with caution in bronchospastic airway disease.<br><br>For patients with severe bronchospastic airway disease other forms of nicotine replacement are recommended. | |
| **Lozenge** | 2 and 4 mg<br><br>Nicorette®, generic | *Based on time to 1st cigarette of day:*<br>>30 min – 2 mg<br><30 min – 4 mg<br><br>Weeks 1-6: 1 piece every 1-2 h (Use at least 9 lozenges/day for the first 6 weeks of therapy to improve success rate)<br>Weeks 7-9: 1 piece every 2-4 h<br>Weeks 10-12: 1 piece every 4-8 h<br><br>MDD: 20 lozenges<br><br>Duration: 12 weeks | Allow lozenge to slowly dissolve in the mouth over 20 to 30 minutes, occasionally moving from one side of mouth to other.<br><br>Do not eat or drink for 15 minutes before or during use.<br><br>Do not chew or swallow the lozenge. | Nausea, hiccups, heartburn, headache, cough | Use with caution in patients with dental disease<br><br>Use with caution in patients on a sodium-restricted diet (18 mg of sodium/lozenge) | |

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|---|---|---|---|---|---|---|
| **Products*** | **Availability** | **Dosage** | **Administration** | **Common Side Effects** | **Warnings and Precautions** | **Additional Concerns**** |
| **Nasal spray** | 10 mL metered spray bottle, 10 mg/mL<br><br>Each actuation delivers 0.5 mg of nicotine<br><br>Nicotrol® NS | 1 to 2 doses per h<br>(1 dose = 1 spray in each nostril)<br><br>MDD: 40 doses<br><br>Duration: 3 months | Administer with head tilted slightly back; do not sniff or inhale while spraying. | Nasal irritation, headache, back pain, dyspepsia, constipation | Avoid in severe reactive airway disease and chronic nasal disorders | |
| **Patch** | 7 mg/24 h,<br>14 mg/24 h,<br>21 mg/24 h<br><br>Nicoderm CQ®, generic | *Based on CPD:*<br><10: 14 mg daily for 4-6 wks, then 7 mg daily for 2 wks<br>>10: 21 mg daily for 4-6 wks, then 14 mg daily for 2 wks, then 7 mg daily for 2 wks<br><br>Duration: 10 wks | At start of each day, apply new patch on relatively hairless location between neck and waist. Wash hands after applying or removing patch.<br><br>Rotate site to reduce local skin irritation.<br><br>The patch may be worn for 16-24 h. If patient craves a cigarette first thing in the morning the patch can be worn for up to 24 h. If the patient has vivid dreams or other sleep disturbances, remove before bedtime and apply new patch in the morning. | Skin reactions, headache, insomnia, vivid dreams | If skin redness does not subside after 4 days, or rash or swelling occurs, discontinue use.<br><br>Contains aluminum; remove before MRI.<br><br>Patches should not be cut.<br><br>Patients should only apply 1 patch during a 24 h period. | |

CPD=cigarettes per day; h= hours; MDD=maximum daily dose; MRI=magnetic resonance imaging; wks= weeks
*The gum, lozenge, and patch are available over-the-counter, while the inhaler and nasal spray are available by prescription only.
**These concerns apply to all nicotine replacement therapies.

| Table 3: Non-Nicotine Pharmacologic Agents[1-4,7,8] | | | | | |
|---|---|---|---|---|---|
| **Products*** | **Availability** | **Mechanism of Action** | **Dosage and Administration** | **Side Effects** | **Other Safety Concerns** |
| **Bupropion SR** | 150 mg tablets<br><br>Zyban®, generic | Aminoketone antidepressant<br><br>Inhibition of noradrenergic or dopaminergic neuronal uptake and nicotinic acetylcholinergic receptors | 150 mg PO every morning for 3 days, then 150 mg twice daily (at least 8 h apart)<br><br>MDD 300 mg; reduce dose to 150 mg every other day in patients with moderate-to-severe hepatic impairment (Child-Pugh B or C). Consider reducing the dose or frequency in patients with mild hepatic impairment (Child-Pugh A) or renal impairment (GFR <90 mL/min)<br><br>Duration: 7-12 wks, up to 6 months<br><br>Therapy should be initiated before the patient's planned quit day, while the patient is still smoking. The targeted quit day should be within the first 2 weeks of bupropion SR therapy. It takes approximately 1 week of treatment to reach steady-state.<br><br>May be used in combination with nicotine replacement transdermal system | Headache, insomnia, dry mouth, dizziness, tachycardia, hypertension, anxiety, nausea, arthralgia | Contraindications:<br>• Seizure disorders<br>• Current/history of anorexia/bulimia<br>• Abrupt discontinuation of alcohol, benzodiazepines, barbiturates, antiepileptic drugs<br>• Do not use MAOIs with bupropion or within 14 days of stopping treatment with bupropion.<br>• Do not use bupropion within 14 days of stopping a MAOI.<br>• Do not initiate bupropion in patients being treated with linezolid or intravenous methylene blue<br><br>*Boxed warning*: increased risk of suicidal thoughts; neuropsychiatric events<br><br>Precautions:<br>• Increased seizure risk<br>• Hypertension: Monitor BP, especially if used concurrently with nicotine replacement<br>• Activation of mania/hypomania<br>• Psychosis and other neuropsychiatric reactions<br>• Angle-closure glaucoma has occurred in patients with untreated anatomically narrow angles treated with antidepressants |
| **Varenicline** | 0.5 and 1 mg tablets<br><br>Chantix® | Partial agonist of α4β2 neuronal nicotinic acetylcholine receptors | Days 1-3: 0.5 mg PO daily<br>Days 4-7: 0.5 mg PO twice daily<br>Days 8+: 1 mg PO twice daily<br><br>MDD 2 mg; reduce dose in severe renal dysfunction (estimated CrCl <30 mL/minute)<br><br>Duration: 12 weeks; additional course of 12 weeks can increase long-term abstinence<br><br>Begin varenicline 1 wk before targeted quit date OR begin varenicline and then quit smoking between days 8 and 35 of varenicline treatment<br><br>Concomitant use of varenicline with nicotine replacement therapy potentially can increase incidence of adverse events | Nausea, vomiting, constipation, flatulence, headache, insomnia, abnormal dreams, suicidal ideation | *Boxed warning*: serious neuropsychiatric events<br><br>Precautions:<br>• New or worsening seizures.<br>• Increased effects of alcohol have been reported.<br>• Use caution driving or operating machinery until patient knows how varenicline therapy will affect them.<br>• New or worsening cardiovascular symptoms.<br>• Angioedema and hypersensitivity reactions.<br>• Serious skin reactions.<br>• Nausea is most common adverse reaction and a dose reduction may be needed. |

BP=blood pressure; CrCl=creatinine clearance; GFR=glomerular filtration rate; MAOI=monoamine oxidase inhibitor; MDD=maximum daily dose; PO=by mouth; SR=sustained-release

## Special Populations

Special populations for whom the evidence supporting use of medications is inadequate include adolescents, light smokers, smokeless tobacco users, and pregnant women.[1]

**Table 4: Guideline Recommendations for Pregnant Smokers**

| Guideline | Recommendation |
|---|---|
| AHRQ (2008)[1] | 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.<br><br>Although abstinence early in pregnancy will produce the greatest benefits to the fetus and expectant mother, quitting at any point in pregnancy can yield benefits. Therefore, clinicians should offer effective tobacco dependence interventions to pregnant smokers at the first prenatal visit as well as throughout the course of pregnancy. |
| USPSTF (2015)[2] | Clinicians should ask all pregnant women about tobacco use, advise them to stop using tobacco, and provide behavioral interventions for cessation to pregnant women who use tobacco. Current evidence is insufficient to assess the balance of benefits and harms of pharmacotherapy interventions for tobacco cessation in pregnant women. |

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