

PHARMACOLOGIC PRODUCT GUIDE: FDA-Approved Medications for Smoking Cessation

NICOTINE REPLACEMENT THERAPY (NRT) FORMULATIONS						BUPROPION SR	VARENICLINE
PRODUCT	GUM	LOZENGE	TRANSDERMAL PATCH	NASAL SPRAY	ORAL INHALER		
	Nicorette, ¹ ZONNIC, ² Generic OTC 2 mg, 4 mg original, cinnamon, fruit, mint	Nicorette Lozenge, ¹ Nicorette Mini Lozenge, ¹ Generic OTC 2 mg, 4 mg; cherry, mint	NicoDerm CQ, ¹ Generic OTC (NicoDerm CQ, generic) Rx (generic) 7 mg, 14 mg, 21 mg (24-hr release)	Nicotrol NS ³ Rx Metered spray 10 mg/mL aqueous solution	Nicotrol Inhaler ³ Rx 10 mg cartridge delivers 4 mg inhaled vapor	Zyban ¹ , Generic Rx 150 mg sustained-release tablet	Chantix ³ Rx 0.5 mg, 1 mg tablet
PRECAUTIONS	<ul style="list-style-type: none"> Recent (≤ 2 weeks) myocardial infarction Serious underlying arrhythmias Serious or worsening angina pectoris Temporomandibular joint disease Pregnancy⁴ and breastfeeding Adolescents (<18 years) 	<ul style="list-style-type: none"> Recent (≤ 2 weeks) myocardial infarction Serious underlying arrhythmias Serious or worsening angina pectoris Pregnancy⁴ and breastfeeding Adolescents (<18 years) 	<ul style="list-style-type: none"> Recent (≤ 2 weeks) myocardial infarction Serious underlying arrhythmias Serious or worsening angina pectoris Pregnancy⁴ (Rx formulations, category D) and breastfeeding Adolescents (<18 years) 	<ul style="list-style-type: none"> 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 Pregnancy⁴ (category D) and breastfeeding Adolescents (<18 years) 	<ul style="list-style-type: none"> Recent (≤ 2 weeks) myocardial infarction Serious underlying arrhythmias Serious or worsening angina pectoris Bronchospastic disease Pregnancy⁴ (category D) and breastfeeding Adolescents (<18 years) 	<ul style="list-style-type: none"> Concomitant therapy with medications/conditions known to lower the seizure threshold Hepatic impairment Pregnancy⁴ (category C) and breastfeeding Adolescents (<18 years) Treatment-emergent neuropsychiatric symptoms⁵: <p>BOXED WARNING REMOVED 12/2016</p> <p>CONTRAINDICATIONS:</p> <ul style="list-style-type: none"> 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 	<ul style="list-style-type: none"> Severe renal impairment (dosage adjustment is necessary) Pregnancy⁴ (category C) and breastfeeding Adolescents (<18 years) Treatment-emergent neuropsychiatric symptoms⁵: <p>BOXED WARNING REMOVED 12/2016</p>
DOSING	<p>1st cigarette ≤30 minutes after waking: 4 mg</p> <p>1st cigarette >30 minutes after waking: 2 mg</p> <p>Weeks 1-6: 1 piece q 1-2 hours</p> <p>Weeks 7-9: 1 piece q 2-4 hours</p> <p>Weeks 10-12: 1 piece q 4-8 hours</p> <ul style="list-style-type: none"> Maximum, 24 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 	<p>1st cigarette ≤30 minutes after waking: 4 mg</p> <p>1st cigarette >30 minutes after waking: 2 mg</p> <p>Weeks 1-6: 1 lozenge q 1-2 hours</p> <p>Weeks 7-9: 1 lozenge q 2-4 hours</p> <p>Weeks 10-12: 1 lozenge q 4-8 hours</p> <ul style="list-style-type: none"> Maximum, 20 lozenges/day Allow to dissolve slowly (20-30 minutes for standard; 10 minutes for mini) 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 	<p>≥10 cigarettes/day: 21 mg/day x 4-6 weeks 14 mg/day x 2 weeks 7 mg/day x 2 weeks</p> <p>≤10 cigarettes/day: 14 mg/day x 6 weeks 7 mg/day x 2 weeks</p> <ul style="list-style-type: none"> 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) Duration: 8-10 weeks 	<p>1-2 doses/hour (8-40 doses/day)</p> <p>One dose = 2 sprays (one in each nostril); each spray delivers 0.5 mg of nicotine to the nasal mucosa</p> <ul style="list-style-type: none"> Maximum <ul style="list-style-type: none"> - 5 doses/hour or - 40 doses/day For best results, initially use at least 8 doses/day Do not sniff, swallow, or inhale through the nose as the spray is being administered Duration: 3-6 months 	<p>6-16 cartridges/day Individualize dosing; initially use 1 cartridge q 1-2 hours</p> <ul style="list-style-type: none"> Best effects with continuous puffing for 20 minutes Initially use at least 6 cartridges/day 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 	<p>150 mg po q AM x 3 days, then 150 mg po bid</p> <ul style="list-style-type: none"> 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 	<p>Days 1-3: 0.5 mg po q AM</p> <p>Days 4-7: 0.5 mg po bid</p> <p>Weeks 2-12: 1 mg po bid</p> <ul style="list-style-type: none"> 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

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ADVERSE EFFECTS	<ul style="list-style-type: none"> Mouth/jaw soreness Hiccups Dyspepsia Hypersalivation Effects associated with incorrect chewing technique: <ul style="list-style-type: none"> – Lightheadedness – Nausea/vomiting – Throat and mouth irritation 	<ul style="list-style-type: none"> Nausea Hiccups Cough Heartburn Headache Flatulence Insomnia 	<ul style="list-style-type: none"> Local skin reactions (erythema, pruritus, burning) Headache Sleep disturbances (insomnia, abnormal/vivid dreams); associated with nocturnal nicotine absorption 	<ul style="list-style-type: none"> Nasal and/or throat irritation (hot, peppery, or burning sensation) Headache Rhinitis Tearing Sneezing Cough Headache 	<ul style="list-style-type: none"> Mouth and/or throat irritation Cough Headache Rhinitis Dyspepsia Hiccups 	<ul style="list-style-type: none"> Insomnia Dry mouth Nervousness/difficulty concentrating Nausea Dizziness Constipation Rash Seizures (risk is 0.1%) Neuropsychiatric symptoms (rare; see PRECAUTIONS) 	<ul style="list-style-type: none"> Nausea Sleep disturbances (insomnia, abnormal/vivid dreams) Constipation Flatulence Vomiting Neuropsychiatric symptoms (rare; see PRECAUTIONS)
ADVANTAGES	<ul style="list-style-type: none"> 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 	<ul style="list-style-type: none"> 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 	<ul style="list-style-type: none"> 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 hours 	<ul style="list-style-type: none"> Can be titrated to rapidly manage withdrawal symptoms Can be used in combination with other agents to manage situational urges 	<ul style="list-style-type: none"> Might serve as an oral substitute for tobacco Can be titrated to manage withdrawal symptoms Mimics hand-to-mouth ritual of smoking Can be used in combination with other agents to manage situational urges 	<ul style="list-style-type: none"> Twice-daily oral dosing is simple and associated with fewer adherence problems Might delay weight gain Might be beneficial in patients with depression Can be used in combination with NRT agents 	<ul style="list-style-type: none"> Twice-daily oral dosing is simple and associated with fewer adherence problems Offers a different mechanism of action for patients who have failed other agents
DISADVANTAGES	<ul style="list-style-type: none"> Need for frequent dosing can compromise adherence Might be problematic for patients with significant dental work Proper chewing technique is necessary for effectiveness and to minimize adverse effects Gum chewing might not be acceptable or desirable for some patients 	<ul style="list-style-type: none"> Need for frequent dosing can compromise adherence Gastrointestinal side effects (nausea, hiccups, heartburn) might be bothersome 	<ul style="list-style-type: none"> 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) 	<ul style="list-style-type: none"> Need for frequent dosing can compromise adherence Nasal administration might not be acceptable or desirable for some patients; nasal irritation often problematic Not recommended for use by patients with chronic nasal disorders or severe reactive airway disease 	<ul style="list-style-type: none"> Need for frequent dosing can compromise adherence Cartridges might be less effective in cold environments ($\leq 60^{\circ}\text{F}$) 	<ul style="list-style-type: none"> Seizure risk is increased Several contraindications and precautions preclude use in some patients (see PRECAUTIONS) Patients should be monitored for potential neuropsychiatric symptoms⁵ (see PRECAUTIONS) 	<ul style="list-style-type: none"> Should be taken with food or a full glass of water to reduce the incidence of nausea Patients should be monitored for potential neuropsychiatric symptoms⁵ (see PRECAUTIONS)
COST/DAY ⁶	2 mg or 4 mg: \$1.90–\$3.70 (9 pieces)	2 mg or 4 mg: \$3.36–\$3.78 (9 pieces)	\$1.52–\$3.48 (1 patch)	\$6.67 (8 doses)	\$11.35 (6 cartridges)	\$2.58–\$7.87 (2 tablets)	\$11.86 (2 tablets)

¹ Marketed by GlaxoSmithKline.

² Marketed by Nicovom USA (a subsidiary of Reynolds American, Inc.)

³ Marketed 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 Wholesale acquisition cost from Red Book Online. Thomson Reuters, December 2016.

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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