Appendix Three: Pharmacotherapy for Smoking Cessation in Patients with Stroke and TIA

This table provides a summary of the pharmacotherapeutic properties, side effects, drug interactions and other important information on the current medications available for use in Canada. This table should be used as a reference guide by health care professionals when selecting an appropriate agent for individual patients. Patient compliance, patient preference and/or past experience, side effects, and drug interactions should all be taken into consideration during decision-making, in addition to other information provided in this table and available elsewhere regarding these medications.

	Nicotine patch	Nicotine gum	Nicotine inhaler	Nicotine Lozenge	Bupropion	Varenicline
Initial Treatment Length	8-12 weeks	4-36 weeks	12-24 weeks	4-24 weeks	7-12 weeks	12 -24 weeks
Time to Peak Effect	Requires 2-3 days to get maximal serum levels	After 20-30 min of chewing	Within 15 minutes after forced inhalation for 20 minutes	After 20-30 min of sucking	1-2 weeks	1-2 weeks
Indications	As an aid to smoking cessation				As an aid to smoking cessation, major depressive disorder, seasonal affective disorder	As an aid to smoking cessation
usual Dosing	24 Hour patch: 21 mg for 3 to 6 weeks, then 14 mg for 2 to 4 weeks then 7 mg for 2 to 4 weeks. 16 Hour patch: 15mg for 6 weeks then10mg for 2 weeks then 5mg for 2 weeks	<25 cig/d or smokes >30 min upon waking: 2 mg >25 cig/d or smokes <30 min upon waking: 4 mg Week 1-6; 1 piece q1-2h (at least 9/d) Week 7-9: 1 piece q2-4h Week 10-12: 1 piece q4-8h Stop when reduced to 1-2 per day Max: 20-30 pieces per day	Weeks 1-12: 6-12 cartridges per day then gradually reduce as able. (min 6/d for first 3-6 weeks) Stop when reduced to 1-2 per day Max: 12 cartridges per day	Polacrilex: Smokes >30 min upon waking: 2mg Smokes <30 min upon waking: 4mg Bitartarate: < 20 cig/d: 1 mg > 20 cig/d: 2 mg Week 1-6; 1 lozenge q1-2h Week 7-9: 1 piece q2-4h Week 10-12: 1 piece q4-8h Stop when reduced to 1-2 per day Max: 30 mg/day	150 mg once daily x 3 days then 150 mg BID x 7-12 weeks. Begin 1-2 weeks prior to selected quit date	0.5 mg once daily x 3 days then 0.5 mg BID x 4 days then 0.5-1 mg BID x 12 weeks. Begin 1-2 weeks prior to selected quit date.
Special Dosing Notes	Smokers are precise in the way they titrate their smoking to maintain nicotine levels, and dosing should be titrated and personalized accordingly. A common issue is under dosing NRT in heavier smokers. Dosing guide: 1 cigarette = 1 mg nicotine. E.g., if smoke 2 packs per day, offer 2 x 21mg patches plus gum or				Must titrate dose when discontinuing	Upward titration to reduce nausea from drug

	Nicotine patch	Nicotine gum	Nicotine inhaler	Nicotine Lozenge	Bupropion	Varenicline
	inhaler for cravings. In the "Reduce to Quit" approach, patients may continue to smoke while on the patch as they are receiving nicotine via the patch/gum/lozenge/inhaler and should be smoking fewer cigarettes, which is the goal.					
Side Effects	Headache, GI upset, dizziness, nausea, disturbed sleep, rash at site	Headache, GI upset, hiccups, disturbed sleep, sore jaw	Irritation of throat and nasal passages, sneezing, coughing especially in those with bronchospastic disease, hiccups	GI upset, mouth/throat soreness, hiccups	Dry mouth, insomnia, agitation, vivid dreams, unease. Risk of seizure is 1/1000 (risk factors include those with seizure or eating disorders)	Nausea, insomnia, abnormal/vivid dreams. Health Canada warning for psychiatric effects
Effect of Food and Other Administration Notes	Do not cut patch, causes rapid evaporation rending product useless. Rotate patch site to avoid skin irritation.	Recent food and beverage impairs release of nicotine. Avoid food and drink 15 min before or while using gum (30 min for caffeine/acidic products). Not regular chewing gum; use bite, chew, park technique.	Not a true inhaler (is a vaporizer) so best effect with continuous puffing; nicotine absorbed from oral mucosa. Cold temperatures can decrease absorption rate.	Recent food and beverage impairs release of nicotine. Avoid food and drink 15 min before or while using lozenge.	Sustained release product; do not crush or chew.	No food cautions.
Drug Interactions	Nicotine itself is not subject to cytochrome P-450 interactions.Tobacco smoke however leads to potent induction of CYP1A1 and 1A2. When smoking is discontinued, the substrate drug may require a dosage decrease over a period of several days. CYP1A1, 1A2 substrates include: theophylline, clozapine, olanzapine, fluvoxamine, TCAs (partial substrate).				Inhibits CYP2D6, 2B6 substrate, avoid with MAOI	Increased adverse effects if combined with NRT
Contraindications/ Cautions	Life-threatening arrhythmias, severe angina, atopic/eczematous dermatitis or other skin conditions (e.g. psoriasis)	Life-threatening arrhythmias, severe angina	Life-threatening arrhythmias, severe angina	Life-threatening arrhythmias, severe angina	Seizure disorder, anorexia, bulimia, use of MAOI in 14 days, patients undergoing abrupt discontinuation of alcohol, sedatives and benzodiazepines	Depression, suicidal ideation, schizophrenia, bipolar other major depressive disorders *See Note below

	Nicotine patch	Nicotine gum	Nicotine inhaler	Nicotine Lozenge	Bupropion	Varenicline
Use in Special Populations	• Cardiovascular/Stroke Patients: Demonstrated safety in stable cardiovascular disease (possible exceptions are unstable angina, recent MI, unstable arrhythmia, acute heart failure). Commonly used in many inpatient settings as symptoms of nicotine withdrawal can begin within 1 hour. It is considered by many experts as far safer than continued smoking. • Pregnancy/Breastfeeding/Adolescents: While data are limited in pediatrics and pregnant/breastfeeding women, NRT is generally considered safer than smoking in these populations and should be considered. Offer the lowest effective dose of a short-acting nicotine product to minimize nicotine exposure.				May be used in pregnant women, especially those with depression. May be considered in adolescents or breastfeeding women. Requires dose adjustment in renal/hepatic disease.	Data not available in pregnancy/lactation. May be considered in adolescents. Requires dose adjustment in renal disease (if CrCl<30mL/min, max 0.5 mg BID).
Combination Therapy?	Can use with oral agents, gum, inhaler or lozenges. Evidence suggests better abstinence rates with combination over monotherapy.	Can use with oral agents or patch. Evidence suggests better abstinence rates with combination over monotherapy.			Can use with varenicline or NRT (nicotine replacement therapy). Addition of patch significantly increases long term cessation compared with patch alone. Monitor for treatment emergent hypertension when NRT is combined with bupropion.	Can use with bupropion or NRT (although increased adverse effects with NRT).
Mechanism of Action	Partially replaces nicotine delivered by cigarettes				Not fully understood. Likely due to inhibition of dopamine and norepinephrine uptake.	Partial agonist at nicotinic acetylcholine receptor, causing decreased dopamine release and activation of mesolimbic reward system.
Approximate $ per month	$100	$75-200 (6-20 pieces/d)	$175- 350 (6-12 cartridges/d)	$100-250 (6-12 lozenges/d)	$60	$125

**** Note:*** *on September 14, 2016, a joint meeting of the U.S. Food and Drug Administration's (FDA) Psychopharmacologic Drugs Advisory Committee and Drug Safety Risk Management Advisory Committee reviewed data from EAGLES (Evaluating Adverse Events in a Global Smoking Cessation Study) evaluating the neuropsychiatric safety of Champix® (varenicline) to determine whether the findings support changes to the product labeling in the US. By a majority vote, the Advisory Committee recommended to remove the boxed warning regarding serious neuropsychiatric adverse events from the labeling. At the time of pubictaion of these recommendations, Canadian product monographs have not changed.*