**Appendix C**

# Pharmacotherapy Guide for Smoking Cessation Medications

| | ZYBAN | GUM OR LOZENGE | NICOTINE PATCH | Varenicline |
|---|---|---|---|---|
| **DOSING** | 150 mg QAM for 3 days then increase 150 mg BID<br><br>-Renal failure and mild to moderate cirrhosis: may necessitate reduced dose and frequency<br>-Severe cirrhosis: dose should not exceed 150mg every other day | **Combination Therapy:**<br>• Use for acute episodes of craving or tapering of patch<br>**Monotherapy:** fixed schedule preferred to prn use<br>Gum:<br>• 2mg if <25 cigarettes per day<br>• Weeks 1-6: 1 every 1 to 2 hrs not more than 24/day<br>7-9: 1 every 2-4 hours<br>10-12: 1 every 4-8 hours<br>Lozenge:<br>• 2mg if first cigarette after 30 min of waking<br>• Weeks 1-6: 1 every 1-2 hours not more than 20/day<br>7-9: 1 every 2-4 hours<br>10-12: 1 every 4-8 hours | **Standard dosing schedule:**<br>• 21 mg/day X 4-6 weeks<br>• 14mg/day X 2 weeks<br>• 7mg/day X 2 weeks<br><br>**Individualize drug dose:**<br>• <10 cig/day consider lower starting dose<br>• heavy smokers consider high dose patches with note possible increase side effects e.g. rash and nicotine toxicity<br>Dose to approximate pts nicotine usage<br>eg. 1 cig ≅ 1mg nicotine | Treatment days — Dose<br>Days 1 to 3 — White tablet (0.5 mg), 1 tablet each day<br>Days 4 to 7 — White tablet (0.5 mg) twice a day (1 in the morning and 1 in the evening)<br>Day 8 to end of treatment — Blue tablet (1 mg) twice a day (1 in the morning and 1 in the evening)<br>• Severe renal function impairment (est CrCl <30ml/min)=Starting dose is 0.5 mg once daily, then titrate as needed to a maximum dosage of 0.5 mg twice daily.<br>• ESRD undergoing hemodialysis=max dose of 0.5 mg once daily may be administered if tolerated well |
| **CONTRA-INDICATIONS** | • Seizures disorder<br>  • Epilepsy or febrile childhood seizure<br>• Serious brain injury<br>  • Closed head trauma (see appendix)<br>  • Stroke<br>  • Brain surgery<br>• Eating disorders<br>  • Anorexia nervosa or bulimia<br>• MAO inhibitors<br>• Undergoing abrupt d/c of alcohol or sedatives | • Active temporomandibular joint (TMJ) disease | • Allergy to tape | • None determined |
| **PRECAUTIONS** | • Liver Disease<br>• Renal Disease<br>• Medications which lower seizure threshold | • Recent MI, severe angina pectoris, life threatening arrhythmias, active stomach ulcer<br>• Phenylketonurics (lozenge contains aspartame) | • Recent MI, severe angina pectoris, life threatening arrhythmias | • Severe renal function impairment or ESRD |
| **PREGNANCY** | • CLASS B | • CLASS C/D | • CLASS C/D | • Class C |
| **SIDE EFFECTS** | ➢ Insomnia<br>➢ Dizziness<br>➢ Anxiety<br>➢ Agitation<br>➢ Dry mouth<br>➢ Headache | ➢ Local irritation in throat and mouth<br>➢ Coughing<br>➢ Nausea<br>➢ Hiccups | ➢ Localized rash<br>➢ Insomnia<br>➢ Abnormal dreams/nightmares<br>➢ Dizziness | ➢ Nausea,<br>➢ Vomiting<br>➢ Sleep disturbance<br>➢ Constipation<br>➢ Flatulence<br>➢ Vomiting |
| **PATIENT EDUCATION** | ✓ Start Zyban 1 week before quit date<br>✓ Allow at least 8 hours between successive doses<br>✓ Alcohol and drowsiness warning | ✓ Avoid acidic beverages<br>**Patient instruction for nicotine lozenge:**<br>✓ Once placed in mouth move from one side to the other until completely dissolved<br>✓ Don't chew or swallow<br>**Patient instructions for nicotine gum:**<br>✓ Chew gum slowly until "peppery" or "minty" taste emerges, then "park" between cheek and gum<br>✓ Repeat cycle of chewing and parking for ~30 minutes or until taste dissipates | ✓ Apply patch to a clean, dry, hairless site on arms or torso<br>✓ Wash hands before and after handling patch, while disposing in provided tray<br>✓ Apply every morning to a different site and replace in 24 hours<br>✓ If vivid dreams occur may remove at bedtime<br>✓ Do not shave area before applying patch | ✓ Start varenicline 1 week before quit date<br>✓ Take after eating and with a full glass of water<br>✓ Patients who cannot tolerate the adverse reactions of varenicline may have the dose lowered temporarily or permanently |

**Appendix D**

**Screening questions for head trauma suggesting a predisposition to seizures years after event** [4,5]

1) Have you had closed head trauma resulting in any loss of consciousness or amnesia within the past 5 years?
2) Have you had closed head trauma at any time resulting in resulting in loss of consciousness or amnesia for >30 minutes?
3) Have you had closed head trauma at any time resulting in skull fracture?
4) Have you had closed head trauma at any time resulting in a subdural hematoma or brain contusion?

- Strongest risk factors for post-traumatic seizures persisting for at least **20 years** in patients with:
  - brain contusion
  - subdural hematoma
- Moderate (two-fold) increase in the risk of post-traumatic seizures for at least **5 years** in patients with:
  - mild closed head injury and loss of consciousness or post-traumatic amnesia <30 minutes

**Pregnancy** [1,13,14]

In 2001 twelve percent of all women giving birth in the US reported smoking throughout pregnancy despite the obvious risk. Women can reduce the risks of smoking-related complications to almost the nonsmoker level if they quit during the first trimester. Treatment remains controversial due to variation in pregnancy categories and lack of clinical trials.

The FDA assigned pregnancy categories vary depending on the reference. For instance, USPHS guidelines list all NRT products to be category D with the exception of the patch which is category C. Facts and Comparisons is the opposite with all NRT products Category D with the nicotine gum being Category C.

To date no clinical efficacy trials have addressed bupropion use in pregnancy. Two studies with the nicotine patch have been conducted and neither showed increase in cessation rate possibly due to inadequate levels of nicotine replacement due to faster metabolism.

The harmful effects of cigarette smoking on maternal and fetal health are clearly established, however some studies have shown that nicotine itself is neuroteratogenic so treatment with nicotine replacement therapy should be guided by the following recommendations:

- Use medication doses that are at the low end of the effective dose range e.g. 7 and 14mg patch and the 2mg gum
- Intermittent rather than continuous drug exposure is preferred e.g., nicotine gum rather than the nicotine patch and if patch is used remove at bedtime since 16mg hour dosing is as effective as 24 hour thus minimizing nicotine exposure
- Begin treatment early in pregnancy as possible preferably in the first instead of second or third trimester which is contrary to classical views of teratogenesis. Nicotine receptors which are the specific target for adverse effects develop after the major phase of systemic organogenesis
- Individualize treatment based on contraindications and mother preference. For instance patients with nausea/vomiting of pregnancy oral NRT may be poorly tolerated

**High dose nicotine patch therapy** [7,9,10,11]

Background:

- More than two dozen studies have been performed with nicotine patches showing doubling or tripling of quit rates, yet absolute cessation rates remain modest
- Possibly due to under dosing of the standard nicotine patch of 21-22mg/d which results in less than 50% of the serum nicotine levels produced by smoking one pack of cigarettes per day
- Light smokers with lower baseline cotinine (nicotine metabolite) levels have higher stop rates, suggesting that their nicotine needs were met
- Small number of clinical trials addressing high dose nicotine patches have shown mixed results in long term abstinence rates though short term rates have been higher thus some experts recommend that heavier smokers may need higher doses to achieve initial abstinence rates. It should be noted that doses above 21mg are not yet FDA approved.

**Treatment of spit tobacco** [12]

- Behavioral interventions are effective
- Bupropion is probably effective
- NRT may be effective

**Initial patch dosing**

| Cig/day | Cans/week | Patch dose (mg/d) |
|---|---|---|
| <10 | 1 | 7-14 |
| 10-20 | | 14-22 |
| 21-40 | 2-3 | 22-44 |
| >40 | >3 | 44+ |

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