Smoking Cessation Pharmacotherapy Guidelines

Introduction
This document is aimed at Specialist Advisors from NHS Wirral Stop Smoking Service (SSS) and Intermediate Advisors who have attended SSS training to help patients stop smoking. It is based on NICE Public Health guidance 10 ‘Smoking cessation services’ (2008), NICE Technology Appraisal 123 ‘Varenicline for smoking cessation (2007), NICE Public Health Guidance 26 ‘Quitting smoking in pregnancy and following childbirth’ (2010) and the Department of Health NHS Stop Smoking Services: Service and Monitoring Guidance 2010/11. It provides guidance on the use of Nicotine Replacement Therapy (NRT), bupropion and varenicline.

The use of NRT, Bupropion and Varenicline
Nicotine Replacement Therapy (NRT), varenicline (Champix) and bupropion (Zyban) are recommended for smokers who have expressed a desire to stop smoking. NRT can be used for clients aged 12 years and over. Varenicline and bupropion should not be used in those under the age of 18 and in women who are pregnant or breastfeeding.

The clinician and patient should choose the medication that seems most likely to succeed, and should not favour one over the other. When deciding which therapies to use and in which order, discuss the options with the client and take into account:

- Contraindications and the potential for adverse effects
- The client’s personal preference
- The availability of appropriate counselling or support
- The likelihood that the client will follow the course of treatment
- Their previous experience of smoking cessation aids

All treatments should only be prescribed as part of an abstinent-contingent treatment (ACT) in which the smoker makes a commitment to stop smoking.

Subsequent prescriptions should only be given to people who have demonstrated, on re-assessment that their quit attempt is continuing.

NRT, bupropion or varenicline should not be prescribed in any combination.

Cigarette smoking can interact with certain medicines. Therefore, the potential for interactions when a person stops or starts smoking should be borne in mind. Not all drug-smoking interactions are clinically significant - see appendix 1 for a list of important interactions.

Please refer to the manufacturer’s Summary of Product Characteristics (SPC) for full prescribing guidance.
NICOTINE REPLACEMENT THERAPY (NRT)

A voucher for NRT can be issued weekly for the first 4 weeks. If at the 4 week follow-up the client has stopped smoking and has not had a cigarette in the 3rd or 4th week, the remaining vouchers can be issued for 2 weekly intervals if required. **A maximum of 12 weeks NRT can be issued in total.**

A combination of nicotine patches and another form of NRT (such as gum, inhalator, lozenge or nasal spray) can be offered to people who show a high level of dependence on nicotine or who have found single forms of NRT inadequate in the past. If combining NRT products e.g. patch plus 2mg gum, the supplementary product should not automatically be issued on each voucher, but only according to need.

**Specific Client Groups**

In 2005 the Working Group of the Committee on Safety of Medicines (CSM) considered the available evidence of the safety and efficacy of NRT products with particular reference to cardiovascular risk, pregnancy and use in under-18s. They concluded that NRT could now be used in these groups but the risks and benefits should be clearly explained and behavioural support options should be encouraged.

**Cardiovascular Disease**

The CSM recommended that in stable cardiovascular disease, NRT presents a lesser hazard than continuing to smoke. Dependent smokers with severe or unstable cardiovascular disease (including hospitalisation with a recent myocardial infarction, severe arrhythmia or recent cerebrovascular accident) should be encouraged to stop smoking with non pharmacological interventions. If this fails, NRT may be considered but as data on safety in this group are limited, initiation should be under **medical supervision**.

Therefore, NHS Wirral recommends that if a client has answered yes to any of the questions in the Initial Assessment Health Questionnaire the Specialist or Intermediate practitioner will approach the client’s GP (with the client’s agreement) for permission to recommend the use of NRT. **Only with the GP’s permission will NRT be recommended and a voucher issued.**

**Use of Nicotine Replacement Therapy by Adolescents of 12-17 years**

NRT can be used by adolescents aged 12-17 years but as there are limited data on the safety and efficacy, duration should be restricted to 12 weeks. Treatment should only be continued for longer than 12 weeks on the advice of a healthcare professional.

The young person should have sufficient maturity to understand about the service they are to receive. Once children reach the age of 16, they are presumed in law to be competent to give consent for themselves. Clients under 16 who have sufficient understanding and intelligence to enable them to understand fully what is involved in a proposed intervention will also have the capacity to consent to that intervention. This is sometimes described as being ‘Gillick competent’.

Written by: Rachael Stevenson, Clinical Effectiveness Pharmacist, NHS Wirral and Carol Corvers, Programme Manager, Stop Smoking Service, NHS Wirral

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Nicotine Replacement Therapy during Pregnancy and Breast-feeding

The data available on the use of NRT in pregnancy and breast-feeding women is limited. To eliminate all possible risks from nicotine a woman would ideally stop smoking without using NRT. However, the risk to the foetus of continued smoking is likely to be greater than any potential risks from NRT. This is because cigarette smoking, in general, delivers more nicotine than NRT does, and it exposes both mother and foetus to many other toxins. In light of this, the Working Group of the Committee on Safety of Medicines (CSM) 2005 and NICE (2010) have advised that pregnant and breastfeeding women, who cannot stop smoking on their own, can use NRT.

NICE recommends that smoking advisors should discuss the risks and benefits of NRT with pregnant women who smoke. Only use NRT if smoking cessation without NRT fails. If they express a clear wish to receive NRT, use professional judgement when deciding whether to offer a prescription.

Pregnancy

The decision to use NRT should be made following a risk-benefit assessment as early in pregnancy as possible. The aim should be to discontinue NRT after 2-3 months. Intermittent forms of NRT are preferable during pregnancy but a patch may be appropriate if nausea and/or vomiting are a problem. A 16 hour patch is preferable to a 24 hour patch and pregnant women who are using nicotine patches should be advised to remove them before going to bed to avoid the administration of nicotine overnight. The dosage of NRT suggested should be kept at a lower level than the pregnant woman would be taking if she had continued to smoke and the therapy be used for the shortest time possible.

Breast-feeding

The amount of nicotine the infant is exposed to from breast milk is relatively small and is less hazardous than the second-hand smoke the infant would otherwise be exposed to if the mother continued to smoke. For breastfeeding mothers, intermittent NRT products are preferred as they will allow the time between NRT use and feeding to be as long as possible to minimise the amount of nicotine in the milk.

Partners and others in the household who smoke

Clear advice should be provided about the danger that other people’s tobacco smoke poses to the pregnant woman and to the baby – before and after birth. Recommend that other members of the household do not smoke around the pregnant woman, mother or baby. This includes not smoking in the house or car. Encourage other members of the household to stop smoking.

Other Cautions

- Uncontrolled hyperthyroidism
- Diabetes Mellitus – monitor blood-glucose concentration closely when initiating treatment
- Phaeochromocytoma
- Oral Preparations only: oesophagitis, gastritis, peptic ulcers
- Patches: skin disorders (patches should not be placed on broken skin)
BUPROPION (ZYBAN)

Bupropion is a prescription-only drug licensed for use in smoking cessation with motivational support. Bupropion can only be issued on prescription and not through the Wirral voucher scheme. However, the Specialist or Intermediate advisor should provide ongoing support, advice and follow-up during the treatment period.

Bupropion should not be used in combination with either NRT or varenicline and should be prescribed subject to the contraindications and precautions listed in the Summary of Product Characteristics (SPC) some of which are listed below.

Contraindications
- History of seizures or of eating disorders, bipolar disorder, a CNS tumour, severe hepatic cirrhosis, patients experiencing acute symptoms of alcohol or benzodiazepine withdrawal, risk factors for seizures (see below)
- Factors that increase the risk of seizures include concomitant administration of drugs that can lower the seizure threshold (e.g., antidepressants, antimalarials [such as mefloquine and chloroquine], antipsychotics, quinolones, sedating antihistamines, systemic corticosteroids, theophylline, tramadol), alcohol abuse, history of head trauma, diabetes, and use of stimulants and anorectics.
- Concomitant administration of Monoamine-oxidase inhibitors (MAOIs)
- Women who are pregnant or breastfeeding
- Patients under 18 years

Cautions
- Elderly patients (max dose 150mg daily)
- Predisposition to seizures (see above)
- Monitor blood pressure before and during treatment

Interactions: Drugs known to lower the seizure threshold (e.g., antipsychotics, antidepressants, antimalarials, tramadol, theophylline, systemic steroids, quinolones and sedating antihistamines), citalopram, MAOIs, antipsychotics, beta blockers, carbamazepine, phenytoin, valproate, ritonavir, theophylline, clozapine, other drugs metabolised by CYP 2D6 or CYP 1A2, other inhibitors or inducers of CYP 2B6. See SPC for full list of interacting drugs.

Dose: Start 1 – 2 weeks before stop date, initially 150mg daily for 6 days then 150mg twice daily (max. daily dose 300mg or 150mg in patients with risk factors for seizures). Bupropion should be used for 7-9 weeks. If at seven weeks no effect is seen, treatment should be discontinued. See BNF / SPC for full prescribing details.

The initial and maintenance prescriptions should be for no more than 4 weeks at a time.
VARENICLINE (CHAMPIX)

Varenicline is a prescription-only drug licensed for use in smoking cessation with motivational support. Varenicline can only be issued on prescription and not through the Wirral voucher scheme. However, the Specialist or Intermediate advisor should provide ongoing support, advice and follow-up during the treatment period.

Varenicline should not be used in combination with either NRT or bupropion and should be prescribed subject to the contraindications and precautions listed in the Summary of Product Characteristics (SPC) some of which are listed below.

Contraindications
- Women who are pregnant or breastfeeding
- Patients under 18 years

Cautions
- History of psychiatric illness (see below)
- Irritability, depression and insomnia on discontinuation

Adverse psychiatric reactions
Psychiatric disorders are the most commonly reported suspected adverse reactions for varenicline in the UK. Depression and suicide-related events have been reported in patients using varenicline who are trying to stop smoking. The Medicines and Healthcare products Regulatory Agency (MHRA) and Commission on Human Medicines have advised that patients who are taking varenicline who develop suicidal thoughts or who develop agitation, depressed mood, or changes in behaviour that are of concern for the doctor, patient, family, or caregiver should stop their treatment and contact their doctor immediately.

Dose: Start 1 -2 weeks before stop date, initially 500mcg once daily for 3 days, increased to 500mcg twice daily for 4 days, then 1mg twice daily for 11 weeks (reduce dose to 500mcg twice daily if not tolerated).

The initial prescription should be for the varenicline 2 week starter pack of 11 x 500mcg tablets and 14 x 1mg tablets. The follow on prescriptions should be for a maximum of 4 weeks treatment at a time.

**Locally it has been agreed that the duration of treatment is 12 weeks and that it is not appropriate to give an additional 12 week course**

Discontinuation of varenicline may be associated with irritability, an urge to smoke, depression and/or insomnia in up to 3% of patients. The prescriber should inform the patient accordingly and discuss or consider the need for dose tapering over 1 or 2 weeks. (This should be included in the 12 weeks of treatment).

Interactions: No clinically meaningful interactions

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### Appendix 1 – Clinically important drug-smoking interactions*

<table>
<thead>
<tr>
<th>BNF category/ Drug name</th>
<th>Nature of interaction</th>
<th>Clinical relevance</th>
<th>Action to take when stopping smoking</th>
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<tbody>
<tr>
<td><strong>2.8.2 Warfarin</strong></td>
<td>Warfarin is partly metabolised via the enzyme CYP1A2. An interaction with smoking is not clinically relevant in most patients. The dose of warfarin is adjusted according to a patient’s INR (International Normalised Ratio).</td>
<td>Moderate</td>
<td>If a patient taking warfarin stops smoking, their INR might increase so a healthcare professional should monitor the INR more closely. Advise patients to tell the physician managing their anticoagulant control that they are stopping smoking.</td>
</tr>
<tr>
<td><strong>3.1.3 Theophylline</strong></td>
<td>Theophylline is metabolised principally via the enzyme CYP1A2. Smokers require higher doses of theophylline than non-smokers due to theophylline’s shortened half-life and increased elimination. Some reports suggest smokers may need twice the dose of non-smokers.</td>
<td>High</td>
<td>A healthcare professional should monitor plasma theophylline concentrations and adjust the dose of theophylline accordingly. The dose of theophylline may need to be reduced by about one quarter to one third one week after withdrawal. Advise the patient to seek help if they develop signs of theophylline toxicity such as palpitations or nausea.</td>
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<tr>
<td><strong>4.2.1 Chlorpromazine</strong></td>
<td>Chlorpromazine is metabolised principally via CYP1A2. Smokers have lower serum levels of chlorpromazine compared with non-smokers.</td>
<td>Moderate</td>
<td>Monitor by a healthcare professional Be alert for increased adverse effects of chlorpromazine (e.g. dizziness, sedation, extrapyramidal side effects). If adverse effects occur, reduce the dose as necessary.</td>
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<tr>
<td><strong>4.2.1 Clozapine</strong></td>
<td>Clozapine is metabolised principally via CYP1A2 and clearance is increased in smokers. Serum clozapine levels are reduced in smokers compared with non-smokers; smokers may need higher dosages. There have been case reports of adverse effects in patients taking clozapine when they have stopped smoking.</td>
<td>High</td>
<td>Contact Lisa Foulkes (pharmacy team secretary) at Cheshire and Wirral Partnership NHS Foundation Trust (CWP) IMMEDIATELY to be directed to a pharmacist for guidance: Tel: 01244 397 494</td>
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4.2.1 Olanzapine

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<tr>
<th>Olanzapine is metabolised principally via CYP1A2 and clearance is increased in smokers. Serum olanzapine levels are reduced in smokers compared with non-smokers; smokers may need higher dosages.</th>
<th>Moderate</th>
<th>Monitor by a healthcare professional</th>
</tr>
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<tbody>
<tr>
<td>Be alert for increased adverse effects of olanzapine (e.g. dizziness, sedation, hypotension). If adverse reactions occur, reduce the dose as necessary.</td>
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6.1.1 Insulin

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<th>Smoking is associated with poor glycaemic control in patients with diabetes. Smokers may require higher doses of insulin but the mechanism of any interaction is unclear.</th>
<th>Moderate</th>
<th>If a patient with insulin-dependent diabetes stops smoking, their dose of insulin may need to be reduced.</th>
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<tr>
<td>Advise the patient to be alert for signs of hypoglycaemia and to test their blood glucose more frequently.</td>
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