

## 4.1

# Pharmacological Treatment Dimensions Pharmacotherapy

### Overview of Pharmacotherapy

The experience of withdrawal after stopping smoking is an important barrier against successful quitting. The aim of pharmacological treatment in smoking cessation support is to ease the experience of withdrawal, thus making the initial transition from smoking to not smoking easier. Studies in the general population indicate that use of pharmacological treatments significantly increases the likelihood of smoking abstinence being maintained (see section 1.4). Because of this potential, the offer of pharmacotherapy is also likely to increase the numbers of people accessing stop smoking support.

Pharmacotherapy can have its drawbacks, however. For example, no medicine or supplement can completely remove withdrawal symptoms, and the person quitting still needs to deal with the psychological and behavioural challenges of stopping smoking. Second, most pharmacological products used in smoking cessation have side effects. These side effects range from the normally minor complications of nicotine replacement delivery (eg – skin irritations, disrupted sleep) to consequences that, in certain groups of patients, can be life threatening (the potential of bupropion to lower the seizure threshold).

Therefore, while pharmacological aids to smoking cessation have great potential in helping people quit, it is advisable that they are used as part of a professionally supervised quit attempt, together with physical health checks and psychological support. This section discusses the use of the three major forms of smoking cessation pharmacotherapy: nicotine replacement therapy (NRT), bupropion (Zyban) and varenicline (Champix).

### Nicotine Replacement Therapy

By far the most widely used pharmacological treatment in stop smoking support is Nicotine Replacement Therapy (NRT). NRT is designed to replace some of the nicotine previously gained from cigarettes and thereby reduce cravings and other withdrawal symptoms. It is available in a range of forms including: nicotine skin-patches, chewing-gum, lozenges, sublingual tablets, inhalators and nasal spray. Adding Nicotine Replacement Therapy to stop smoking support increases the rate of quitting by 50-70% (Stead et al., 2008).

There are potential side effects associated with using NRT. These include skin irritation (eg- patch), stomach problems (eg- gum, lozenge) or irritation to the eyes and nose (nasal spray). However, NRT is generally considered a non-invasive treatment with few risks to health. In fact, it should be remembered that when a quitting smoker uses nicotine products, they are only consuming something that they have already been consuming in much higher quantities while smoking (ie – nicotine). The main difference is that NRT delivers nicotine without the dangerous chemicals that are also delivered by a cigarette.

While certain patient groups must only be prescribed NRT with caution, (eg – unstable cardiovascular disease, pregnant women) there is little reason to fear that NRT will have side effects among mental health service users over and above the general population. Some concerns may be appropriate about

the misuse of NRT in certain, high secure settings (eg- gum can block locks), but generally speaking NRT represents a relatively safe and practical way of supporting quit attempts in mental health settings.

Indeed, as highlighted by Williams & Foulds (2007), nicotine treatment may have particular advantages for smokers with schizophrenia because it improves abnormal electrophysiological measures, saccadic eye movements, and measures of working memory. This may be particularly true for products that deliver a rapidly absorbed dose of nicotine such as the nasal spray. Benefit has also been gained (in a general population) by combining nicotine patches with more rapidly absorbed products. This combination therapy, in trials, has proved more effective than single product therapy (Stead et al., 2008).

### **Bupropion Hydrochloride (Zyban)**

The first non-nicotine medicine to be licensed as an aid to smoking cessation was bupropion (Zyban). Bupropion is an atypical antidepressant that acts as a noradrenaline and dopamine reuptake inhibitor. As such, it is thought that it helps people to quit smoking by increasing the amount of noradrenaline and dopamine free to act in the brain. Treatment with bupropion should be started at least a week before a smoker's quit date.

Studies of bupropion suggest that it can double the chances of quitting (Hughes et al., 2007). However, while a few research studies have demonstrated that bupropion can be used safely and effectively among mental health service users (eg- Evins et al. 2005), it is rarely used as a quit smoking aid in UK mental health settings. One reason is that it has the potential to lower the seizure threshold and therefore may be dangerous when used in conjunction with other drugs known to have this effect, which include some anti-psychotics and anti-depressants.

### **Varenicline (Chantix)**

Varenicline (Chantix / Chantix) is an alpha4beta2 nicotinic acetylcholine receptor partial agonist that was licensed for the treatment of tobacco dependence in 2006. As such, varenicline works by stimulating the nicotinic receptors in the brain and relieving withdrawal, as well as blocking nicotine from acting on these receptors and hence also interfering with any rewarding effects of a lapse back to smoking. Like bupropion, treatment with varenicline begins before the quit date.

Currently, there is evidence to suggest that varenicline may represent the most effective pharmacological treatment for tobacco addiction. Review level analyses suggest that varenicline increases the odds of cessation by 2.33 (95% CI 1.95 to 2.80) compared with placebo, by 1.52 (95% CI 1.22 to 1.88) compared with bupropion, and by 1.31 (95% CI 1.01 to 1.71) compared with nicotine patches (Cahill et al, 2008).

The potential of varenicline is further boosted by the apparent lack of interactions with other medicines and few side effects (the most common effect in trials was mild to moderate nausea). However, it should be noted that, as a relatively new drug, varenicline has only been extensively tested in 'healthy populations' and more data is needed on its safety and efficacy in groups of patients with chronic medical conditions.

Concern has particularly been voiced about the use of varenicline in people with mental health problems. This concern has not arisen through the results of clinical trials, but rather as a result of widely publicised reports of suicidal thoughts or behaviour in people taking the medicine. These reports, have been reflected in changes to the official guidance on prescribing varenicline (eg – MHRA, 2008). Clinicians are advised to inform patients of the adverse reports of side effects, ensure that appropriate monitoring and support is in place, take particular care in prescribing to patients with a history of mental illness and stop treatment immediately if psychological or behaviour problems emerge.

Clearly, more research evidence is required on the safety and efficacy of varenicline for people with mental health problems. However, data from Stapleton et al (2008) does suggest that varenicline is a valid treatment option in this population. The study sample incorporated a sub-group of 111 smokers (27% of total sample) currently receiving treatment for mental illness (primary diagnoses included depression, bipolar disorder and psychosis). The analysis revealed that varenicline, which produced higher quit rates across the whole sample than NRT, was equally effective in those with and without mental illness. Furthermore, there was no evidence of more adverse symptoms being experienced by those with mental illness, including depression and anxiety.

More recently, (Gunnell et al, 2009) examined 80,660 records of patients prescribed either NRT (63,265), bupropion (6422) and varenicline (10,973). There was no increased risk of suicide, self-harm, suicidal thoughts, or subsequent use of antidepressants in patients using varenicline or bupropion as compared with NRT (the only two suicides found involved patients using NRT). As Foulds (2009) points out, while this study was not conducted in a mental health service setting, it did use a 'real world sample', with 10% having a history of alcohol misuse, 5% using antipsychotic medication, 13% using anti-anxiety medication and 24% antidepressants. Maybe most notably, 11% had experienced a previous suicide related event.

## References

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