

## Efficacy of pharmacotherapy

- Nicotine replacement therapy (NRT) and bupropion are effective for smoking cessation when used as adjunctive therapy within a comprehensive behavioural therapy program
- Evidence on comparative efficacy is limited, but NRT and bupropion appear to produce similar abstinence rates
- A systematic review has found pooled odds ratios of abstinence rates using NRT or bupropion versus placebo, significantly favours either active treatment at 6 or 12 months follow up. NOTE: this pooled outcome is not supported by all individual studies, in particular with complete abstinence rates achieved with bupropion at 12 months.

## Choice of pharmacotherapy

- Comorbidities
- Prior quit attempts using pharmacotherapy
- Concomitant drug therapy
- Patient's preference

## Safety considerations

- Consider potential drug interactions as a consequence of smoking cessation (tobacco smoke induces hepatic enzymes eg.CYP 1A2)
- Adverse effects associated with NRT or bupropion are very similar to those of tobacco withdrawal symptoms ie. headache, anxiety, sweating, confusion, dizziness, aggressiveness, and insomnia

**Table 1. Potential drug interactions when ceasing smoking**

Drug	Effect of smoking cessation and management
Theophylline	Within 7 days of smoking cessation theophylline clearance falls on average by 35%, monitor drug plasma levels and adjust dose if needed. NRT has no effect on theophylline metabolism
Insulin	Insulin requirements may become less and dose may need alteration
Clozapine	May increase clozapine serum levels. Monitor serum drug levels and adjust dose if needed, monitor for potential increase in adverse effects.
Caffeine	Decreased clearance as enzyme induction gradually lost, warn patient of potential transient increased sensitivity to caffeine.

## Bupropion SR (Zyban®)

- 150 mg sustained release (SR) tablet twice a day is the most widely studied and effective dose for smoking cessation when used as adjunctive therapy within a comprehensive behavioural therapy program
- limited or lack of information in smokers with chronic obstructive pulmonary disease, asthma, cardiovascular disease, post traumatic stress disorder, major depression or alcoholism, and for relapse prevention

**Table 2. Safety considerations with bupropion**

<b>Contraindications</b>	Current or any history of seizure disorder, known CNS tumour, abrupt withdrawal from alcohol or benzodiazepines, current or previous bulimia or anorexia nervosa, pregnancy and lactation, hypersensitivity to bupropion, concomitant use of MAOI's
<b>Seizures</b>	Seizure risk: 1 in 1000 and is dose dependent (5 fold increase in seizure risk in doses >450mg/day) Risk increased with concomitant administration of drugs known to lower the seizure threshold (e.g. SSRI's, TCAs, antipsychotics, tramadol, theophylline, quinolones, systemic steroids, sedating antihistamines, antimalarials), stimulants or anorectic agents, excessive use of alcohol or sedatives, diabetes treated with hypoglycaemics or insulin and in patients with a history of head trauma
<b>Other precautions</b>	May precipitate a manic episode in bipolar patients, activate latent psychosis in susceptible patients
<b>Adverse effects (most common)</b>	GI upset, abdominal pain, dry mouth, constipation, insomnia, tremor, concentration disturbance, headache, dizziness, depression, agitation, anxiety, rash, pruritis, sweating, hypersensitivity type reactions, taste disorders.
<b>Drug interactions</b>	<b>Risk of serotonin syndrome</b> with other serotonergic agents (e.g. antidepressants, triptans, tramadol, illicit drugs eg.ecstasy). <b>Increased risk of seizures with drugs that lower the seizure threshold.</b> <b>Bupropion inhibits CYP2D6</b> , increasing the serum concentrations and risk of adverse effects of drugs metabolised via CYP2D6 e.g. metoprolol, propranolol, perhexiline, antipsychotics (eg.risperidone, clozapine, haloperidol), venlafaxine, TCA's, oxycodone, codeine, tramadol, mexiletine <b>Bupropion may increase the incidence of adverse effects of levodopa</b> (e.g. tremor, nausea and vomiting). <b>Protease inhibitors (e.g.ritonavir) may inhibit the metabolism of bupropion</b> , possibly increasing bupropion levels and risk of toxicity, avoid combination. <b>Bupropion decreases cyclosporin plasma concentrations</b> , monitor and adjust dose accordingly if required

