SMOKING CESSATION: EFFECT ON PSYCHOTROPIC DRUGS

Cigarette smoking contributes to inter-individual variations in response to an administered drug. Polycyclic aromatic hydrocarbons (PAHs) present in tobacco smoke induce certain hepatic enzymes, particularly CYP1A2, the enzyme responsible for the metabolism of many therapeutic drugs. Smoking can lower the blood levels of some drugs significantly, affecting both efficacy and adverse effects, and higher doses are often required in smokers than non-smokers.

When people stop smoking, hepatic enzyme activity reduces over a week or so. Nicotine Replacement Therapy has no effect on hepatic enzyme activity, but will have other conflicting physiological effects. Plasma levels of affected drugs will then rise, and dose reduction will usually be necessary. The process is complex and difficult to predict, complicated by the fact that few people manage to give up smoking completely and may smoke intermittently. Close monitoring of clinical progress, adverse effects and, where appropriate, plasma levels are essential.

- Ascertain current smoking status and recent compliance with medication.
- Adjust dose if appropriate taking into consideration: age, hepatic function, half-life of drug.
- Review after 5-7 days – assess for emergence of adverse effects, adjust dose if necessary.
- Follow-up after 14 days – monitor adverse effects and ascertain smoking status, further adjust dose if necessary.

Special care is required for patients taking clozapine and individual advice is available from the Pharmacy Department, Woodland View. Trough plasma levels of clozapine should be assessed before converting to NRT and the dose decreased on starting NRT.

It is important to recognise that patients who temporarily stop smoking in hospital usually resume smoking after discharge and drug dosages may then need to be readjusted.

Clinical relevance of interactions

The majority of interactions are not clinically significant but the potential for interaction should be borne in mind if a patient starts or stops smoking.

HIGH: Clinically relevant interaction: documented interaction with clinically important effects and/or drugs metabolised principally by CYP1A2 and with a narrow therapeutic range.

MODERATE: No or minor clinical effects and/or drugs metabolised partly by CYP1A2 and with a narrow therapeutic range and/or drugs metabolised principally by CYP1A2 and with a wide therapeutic range

LOW: Theoretical interaction without documented cases and/or drugs metabolised partly by CYP1A2 and with a wide therapeutic range.

This list is not exhaustive but includes the most commonly encountered psychotropic drugs affected by changes in smoking status. This information is the best available from the resources available at the date of compiling this document.

Please contact Pharmacy Department, Woodland View (01294 322381) for further advice.

Drug	Interaction with smoking	Clinically significant?	Mechanism of interaction	Management in smoking cessation
Clozapine	**Smoking causes lower plasma levels, by up to 50%**	**Yes – smokers may need higher doses**	**PAHs**	**Check serum levels before and one or two weeks after stopping smoking.** **Monitor for adverse effects.** **Contact Pharmacy Department, Woodland View Pharmacy for patient specific advice.**
Beta-blockers – general	Smoking opposes the beneficial effect on heart rate and blood pressure.	**Yes** – smokers may need higher doses	Nicotine	May need lower doses as nicotine levels reduced with NRT.
Duloxetine	Plasma levels 50% lower in smokers than non-smokers	Yes – smokers may need higher doses	Unknown	May need lower doses on conversion to NRT.
Haloperidol	Smoking causes lower plasma levels, by around 20%	Yes – smokers may need higher doses	PAHs	May need lower doses on conversion to NRT.
Lithium	Smoking may increase lithium levels. (Indirect effect: *Xanthine (caffeine) levels may be reduced which would decrease lithium excretion.)*	Theoretically, yes – smokers may need lower doses	PAHs	Monitor levels weekly. May need higher doses on conversion to NRT.
Methadone	Smoking causes lower plasma levels	Yes – smokers may need higher doses	PAHs	Monitor for signs of opioid toxicity and reduce the dose accordingly
Olanzapine	Smoking causes lower plasma levels	Yes – smokers may need higher doses	PAHs	Monitor for adverse effects. May need lower doses on conversion to NRT.
Phenothiazines eg chlorpromazine, fluphenazine	Smoking may cause lower plasma levels	Yes	PAHs	Monitor for adverse effects e.g. sedation, postural hypotension, EPSE. May need to reduce dose.
Benzodiazepines	Smoker may experience less drowsiness than non-smokers	Not usually clinically significant	Unknown	Effects of benzodiazepines may be enhanced. Monitor closely and consider reducing dose.
Tricyclic antidepressants e.g. amitriptyline, imipramine, clomipramine.	Serum levels fall but free levels rise, minimising the clinical significance	Minimal	Nicotine and PAHs	Monitor for adverse effects e.g. sedation, nausea, dry mouth, pulse and BP. Consider reducing if dosage is high.