Drug interactions with smoking

Many interactions between tobacco smoke and drugs have been identified.
In most cases it is the tobacco smoke, not the nicotine that causes these drug interactions.

Tobacco smoke may interact through either **pharmacokinetic** or **pharmacodynamic** mechanisms. Patients should be **regularly monitored** with regard to their smoking status and extent of cigarette consumption and doses of relevant drugs adjusted accordingly.

Pharmacokinetic:

The polyclyclic aromatic hydrocarbons in tobacco smoke stimulate hepatic enzymes cytochrome (CYP) P450 iso-enzymes (1A1, 1A2, and 2E1), primarily 1A2. Induction of these enzymes (from smoking) may result in an increase in the metabolism of many drugs (that are substrates) and cause a subsequent decrease in plasma levels.

Smoking cessation results in the opposite effect – a decrease in metabolism and an increase in plasma concentrations. Dose adjustment is often required based on clinical presentation and monitoring.

The nicotine specifically in nicotine replacement therapies (NRT) does not affect metabolism of other drugs.

Pharmacodynamic:

Nicotine can counter the pharmacological actions of certain drugs because it activates the sympathetic nervous system.

The amount of tobacco smoking needed to have this effect has yet to be established and therefore the assumption is that any person who smokes is susceptible. This assumption also extends to NRT.

Quit Victoria

Pharmaceutical Society of Australia

This document has been prepared with the assistance of clinical pharmacists from Alfred Health (compiled April 2019). The information contained in this document is correct and up-to-date at the time of publication, but knowledge and literature in this area can develop quickly. As such, users should always consult the literature and drug interaction references and take account of new developments. The information should not be used as a substitute for specific, individualised assistance of a medical practitioner.

DRUG	NATURE OF INTERACTION WITH SMOKING Pharmacokinetic (PK) | Pharmacodynamic (PD)	ACTION UPON CESSATION OF SMOKING	CLINICAL SIGNIFICANCE
Caffeine	**PK:** Increased clearance.	Advise to reduce caffeine by half.	High
Clozapine	**PK:** Increased clearance and decreased plasma concentrations.	Monitor trough plasma concentrations (if possible before stopping smoking and for two weeks after or sooner if adverse effects develop). Be alert for increased adverse effects. Reduce dose if clinically appropriate. Seek specialist advice from treating mental health practitioner.	High
Erlotinib	**PK:** Increased clearance and decreased plasma concentrations (around two-fold).	Reduce dose to initial starting dose if a patient stops smoking. Seek specialist advice. Nb. People who smoke should be encouraged to stop before therapy is initiated.	High
Irinotecan	**PK:** Increased clearance. Reduced exposure in people who smoke may lead to decreased haematological toxicity.	Seek specialist advice. Dosing should be closely monitored.	High
Theophylline	**PK:** Increased clearance and decreased half-life.	Monitor theophylline levels and reduce dose if clinically appropriate. Advise patient to monitor for signs of toxicity (e.g. palpitations, vomiting or nausea). Nb. It may take several weeks for enzyme induction to dissipate.	High
Chlorpromazine	**PK:** Decreased AUC and decreased plasma concentrations.	Be alert for increased adverse effects (e.g. dizziness, sedation, EPSE). Reduce dose if clinically appropriate.	Moderate
Insulin	**Unclear:** Possible decrease in insulin absorption secondary to peripheral vasoconstriction. Smoking may also increase insulin resistance.	Reduce dose if clinically appropriate. Advise patient to be alert for signs of hypoglycaemia and to test their BGLs more frequently.	Moderate
Methadone	**Likely PK/PD:** Nicotine affects the endogenous opioid system.	Be alert for signs of opioid toxicity. Reduce dose if clinically appropriate. Seek specialist advice. Nb. Methadone attenuates nicotine withdrawal.	Moderate
Olanzapine	**PK:** Increased clearance and decreased plasma concentrations.	Be alert for increased adverse effects (e.g. dizziness, sedation and hypotension). Reduce dose if clinically appropriate.	Moderate
Warfarin	**PK:** Increased clearance and decreased plasma concentrations.	Monitor INR closely. Reduce dose if clinically appropriate.	Moderate
Antiplatelet drugs (clopidogrel & prasugrel)	**PK:** Possible higher antiplatelet effect in people who smoke.	Seek specialist advice.	Low
Benzodiazepines	**Likely PD:** Central nervous system (CNS) stimulation by smoking. Nb. Results from pharmacokinetic studies are mixed.	Monitor for adverse effects (enhanced effect of benzodiazepines). Reduce dose if clinically appropriate.	Low
Beta Blockers	**PD:** Smoking opposes the beneficial effects of beta blockers on blood pressure and heart rate.	Monitor for adverse effects. Reduce dose if clinically appropriate.	Low
Haloperidol	**PK:** Decreased plasma concentrations.	Be alert for increased adverse effects (e.g. drowsiness, EPSE and hypotension). Reduce dose if clinically appropriate.	Low
Mirtazapine	**PK:** Decreased plasma concentrations.	Be alert for increased adverse effects (e.g. sedation). Reduce dose if clinically appropriate.	Low
Selective serotonin reuptake inhibitors (SSRIs)	**PK:** Decreased plasma concentrations. Nb. Best evidence for fluvoxamine, duloxetine and escitalopram.	Be alert for increased adverse effects (e.g. drowsiness and dizziness). Reduce dose if clinically appropriate.	Low
Tricyclic antidepressants	**PK:** Decreased plasma concentrations.	Be alert for increased adverse effects (e.g. sedation, dry mouth). Reduce dose if clinically appropriate.	Low

The most clinically significant interactions are provided here. For more information on any of the listed interactions or to search for other drug interactions, please refer to drug interactions references and literature at www.quit.org.au/psa-references