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 side effects develop). Be alert for increased side effects. Dose reductions may be required if clinically appropriate. Seek specialist advice from treating mental health practitioner.	High
Erlotinib	**PK:** Increased clearance and decreased plasma concentrations (around two-fold).	Revert to standard dosing if a patient stops smoking. Seek specialist advice. Nb. People who smoke should be advised to stop before therapy is initiated.	High
Irinotecan	**PK:** Increased clearance and decreased plasma concentrations of active metabolite.	Seek specialist advice. Dosing should be closely monitored.	High
Olanzapine	**PK:** Increased clearance and decreased plasma concentrations.	Be alert for increased side effects (e.g. dizziness, sedation and hypotension). Dose reductions may be required if clinically appropriate. Seek specialist advice from treating mental health practitioner.	High
Pirfenidone	**PK:** Decreased AUC and decreased Cmax.	Seek specialist advice. People who smoke should be advised to stop before therapy is initiated.	High
Riociguat	**PK:** Increased clearance and decreased plasma concentrations.	A dose decrease may be required if a patient stops smoking. Nb. People who smoke should be advised to stop before therapy is initiated.	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, nausea). Nb. It may take several weeks for enzyme induction to dissipate.	High
Chlorpromazine	**PK:** Increased clearance and decreased plasma concentrations.	Be alert for increased side effects (e.g. dizziness, sedation, EPSE). Reduce dose if clinically appropriate.	Moderate
Flecainide	**PK:** Increased clearance and decreased plasma concentrations.	Monitor for side effects (e.g. dizziness, shortness of breath, arrhythmias). Reduce dose if clinically appropriate.	Moderate
Insulin	**Unclear:** Possible decrease in insulin absorption secondary to peripheral vasoconstriction. Smoking may also increase insulin resistance.	Advise patient to be alert for signs of hypoglycaemia and to test their BGLs more frequently. Reduce dose if clinically appropriate.	Moderate
Methadone	**PK:** Metabolism includes 1A2 enzyme. **PD:** Nicotine affects the endogenous opioid system.	Be alert for signs of opioid toxicity (e.g. sedation, dizziness, respiratory depression). Reduce dose if clinically appropriate. Seek specialist advice. Nb. Methadone attenuates nicotine withdrawal.	Moderate
Ropinirole	**PK:** Decreased AUC and decreased Cmax.	Be alert for increased side effects. Reduce dose if clinically appropriate.	Moderate
Warfarin	**PK:** Increased clearance and decreased plasma concentrations.	Monitor for side effects. Monitor INR closely. Reduce dose if clinically appropriate.	Moderate
Antidepressants metabolised by CYP1A2 e.g. fluvoxamine, duloxetine, imipramine	**PK:** Decreased plasma concentrations.	Be alert for increased side effects. Reduce dose if clinically appropriate.	Low
Benzodiazepines	**Likely PD:** CNS stimulation by smoking. Nb. Results from pharmacokinetic studies are mixed.	Monitor for side effects (enhanced effect of benzodiazepines). Reduce dose if clinically appropriate.	Low
Beta Blockers	**PD:** CNS stimulation by smoking opposes the beneficial effects of beta blockers on blood pressure and heart rate.	Monitor for side effects. Reduce dose if clinically appropriate.	Low
Clopidogrel	**PK:** Data is conflicting. Possible higher antiplatelet effect in people who smoke.	Smoking cessation should still be recommended.	Low
Haloperidol	**PK:** Increased clearance and decreased plasma concentrations.	Be alert for increased side effects. Reduce dose if clinically appropriate.	Low
Heparin	**Unclear:** Increased clearance and decreased half-life observed. Smoking has prothrombotic effects.	Monitor for side effects and adjust dose based on APTT as appropriate.	Low
Nintedanib	**PK:** Decreased exposure in people who smoke.	No dosage adjustment required. People should not smoke during use.	Low

References can be found at www.quit.org.au/psa-references

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. People should be **regularly monitored** with regard to their smoking status and extent of cigarette consumption and doses of relevant drugs adjusted accordingly.

Pharmacokinetic:

The polycyclic aromatic hydrocarbons in tobacco smoke stimulate hepatic enzymes cytochrome (CYP) P450 iso-enzymes (1A1, 1A2, 1B1, 2B6 and 2E1). 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. 1A2 is the most clinically significant as many drugs are substrates of 1A2.

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, side effect occurrence and monitoring of plasma levels.

The nicotine specifically in nicotine replacement therapies (NRT) and e-cigarettes 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 and nicotine-containing e-cigarettes.

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This document has been prepared with the assistance of clinical pharmacists and medicine information pharmacists from Alfred Health (compiled October 2020). 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.