Drug interactions with smoking

Many interactions between tobacco smoke and drugs have been identified. In most cases the cause of these drug interactions is the polycyclic aromatic hydrocarbons in tobacco smoke, not the nicotine.

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 isoenzymes (including 1A1, 1A2, 1B1, 2B6, 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.

Nicotine, including in nicotine replacement therapies (NRT) and e-cigarettes/vapes, does not affect the 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/vapes.

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Quit Bayside Health Pharmaceutical Society of Australia

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Drug	Nature of interaction with smoking Pharmacokinetic (PK) | Pharmacodynamic (PD)	Action upon cessation of smoking	Clinical significance
Caffeine	**PK:** Increased clearance and decreased plasma concentrations.	Advise to reduce caffeine by half. Monitor for increased side effects (e.g. headache, jitteriness, restlessness, insomnia).	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). Monitor 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
Olanzapine	**PK:** Increased clearance and decreased plasma concentrations.	Monitor for increased side effects (e.g. dizziness, sedation, 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. Nb. People who smoke should be advised to stop before therapy is initiated.	High
Riociguat	**PK:** Increased clearance and decreased plasma concentrations.	Monitor for increased side effects (e.g. dizziness, headache, nausea, diarrhoea). Dose reductions may be required if clinically appropriate. 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
Agomelatine	**PK:** Increased clearance and decreased plasma concentrations. Nb. The interaction may be more profound in people smoking> 15 cigarettes per day.	Monitor for side effects (e.g. dizziness, sedation, nausea). Reduce dose if clinically appropriate. Seek specialist advice.	Moderate
Chlorpromazine	**PK:** Increased clearance and decreased plasma concentrations.	Monitor for increased side effects (e.g. dizziness, sedation, extrapyramidal side effects). Reduce dose if clinically appropriate.	Moderate

Drug	Nature of interaction with smoking Pharmacokinetic (PK) | Pharmacodynamic (PD)	Action upon cessation of smoking	Clinical significance
Cinacalcet	**PK:** Increased clearance (around 38%) and decreased plasma concentrations.	Seek specialist advice.	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
Fluvoxamine	**PK:** Increased clearance and decreased plasma concentrations.	Monitor for side effects (e.g. nausea, tremor, nystagmus). 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 monitor for signs of hypoglycaemia and to test their BGLs more frequently. Reduce dose if clinically appropriate.	Moderate
Irinotecan	**PK:** Increased clearance and decreased plasma concentrations of active metabolite.	Seek specialist advice. Dosing should be closely monitored.	Moderate
Methadone	**PK:** Increased clearance and decreased plasma concentrations.	Monitor closely and adjust dose if clinically appropriate. Seek specialist advice.	Moderate
Mexiletine	**PK:** Increased clearance and decreased plasma concentrations.	Monitor for side effects (e.g. nausea, tremor, hypotension). Reduce dose if clinically appropriate. Seek specialist advice.	Moderate
Riluzole	**PK:** Increased clearance (20%) and decreased plasma concentrations.	Monitor for side effects (e.g. drowsiness, headache, dizziness). Seek specialist advice.	Moderate
Ropinirole	**PK:** Decreased AUC and decreased Cmax.	Monitor for increased side effects (e.g. nausea, dizziness). Reduce dose if clinically appropriate.	Moderate
Warfarin	**PK:** Increased clearance and decreased plasma concentrations.	Monitor for side effects and increased bleeding. Monitor INR closely. Reduce dose if clinically appropriate.	Moderate
Benzodiazepines	**Likely PD:** CNS stimulation by smoking. Nb. Results from PK studies are mixed.	Monitor for side effects (enhanced effect of benzodiazepines). Reduce dose if clinically appropriate.	Low
Betablockers	**PD:** CNS stimulation by smoking opposes the beneficial effects of beta blockers on blood pressure and heart rate.	Monitor for increased response (e.g. blood pressure, treatment response for angina). 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
Duloxetine, imipramine	**PK:** Decreased plasma concentrations.	Monitor for increased side effects. Reduce dose if clinically appropriate.	Low

Drug	Nature of interaction with smoking Pharmacokinetic (PK) | Pharmacodynamic (PD)	Action upon cessation of smoking	Clinical significance
Haloperidol	**PK:** Increased clearance and decreased plasma concentrations.	Monitor for increased side effects (e.g. drowsiness, extrapyramidal 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