Drug InterACTIONs with Tobacco Smoke

The polycyclic aromatic hydrocarbons (PAHs) found in tobacco smoke induce liver enzymes responsible for the metabolism of drugs (1A2, 2B6, 2E1) resulting in pharmacokinetic drug interactions. Pharmacodynamic drug interactions with the components of tobacco smoke may also occur. When supporting quit attempts, it is important to be familiar with the drugs which are affected by tobacco smoke and may require dose adjustment or increased monitoring when smoking status changes. Narrow therapeutic index drugs should be monitored closely.[1,2,3]

Drug	Effect of smoking	Change with Smoking Cessation	Clinical Significance*	Action
Benzodiazepines[1,2,5] (e.g., Alprazolam, diazepam, clonazepam)	Stimulation from nicotine may reduce sedative effects Increased metabolism may result in lower serum levels	Potential increase in levels with smoking cessation Possible increase in sedation	Low to Moderate	Monitor - may require dosage reductions
Betablockers[1,2,5]	Increased clearance which may lower serum levels Pharmacodynamic interactions may result in less effective antihypertensive and heart rate control	Potential increase in levels with smoking cessation Effectiveness may be enhanced Possible bradycardia and hypotension	Moderate	Monitor - may require dosage reductions
Bendamustine[1]	Smoking may decrease bendamustine concentrations, with an increase in concentrations of its two active metabolites	Theoretical change in concentration of both bendamustine and its active metabolites	Moderate	Manufacturer recommends caution should be used, or alternative treatments considered in individuals who smoke
Caffeine[1,2]	Smoking increases the clearance of caffeine by about 50%	Potential increase in levels with smoking cessation	Moderate	Increased risk of caffeine related side effects (tremor, nausea) Advise patients to reduce caffeine consumption prior to a quit attempt (eg., reduce to half)
Chlorpromazine[1,2]	Smoking can reduce serum levels	Potential increase in levels with smoking cessation	Moderate	Monitor for adverse effects (e.g., hypotension, sedation) May require dosage reductions
Clopidogrel[1,3]	Smoking-related enzyme induction may increase the metabolism of clopidogrel to its active metabolite Effect of clopidogrel is enhanced in individuals who smoke ≥10 cigarettes/day	Effect of clopidogrel may be diminished by smoking cessation	Low to Moderate	Tobacco cessation should still be recommended in at-risk populations needing clopidogrel
Clozapine[1,2,3]	Smoking can increase metabolism and reduce serum levels	Potential increase in levels with smoking cessation	Moderate to High	Closely monitor drug levels and for symptoms of toxicity (e.g., drowsiness, confusion, rapid heart rate) Reduce dose as required to avoid toxicity An average 50% dosage reduction may be required[3]
Duloxetine[2]	Smoking may lower plasma levels	Potential increase in levels with smoking cessation	Low	May need to decrease dose with smoking cessation Monitor for possible increase in side effects (e.g., nausea, vomiting, and tachycardia)
Erlotinib[2,4]	Smoking increases clearance Individuals who smoke may required higher dosages	Potential increase in levels with smoking cessation	Moderate	Individuals who smoke should be advised to quit (according to the manufacturers recommendations) Dosage adjustment may be required
Flecainide[1,5]	Smoking increases clearance Individuals who smoke may required higher dosages	Potential increase in levels with smoking cessation	Low to Moderate	Monitor for adverse effects (e.g., dizziness and visual disturbances) Assess need for dose reduction
Fluphenazine[2]	Smoking may lower plasma levels	Potential increase in levels with smoking cessation	Moderate	Monitor for increased drowsiness, extrapyramidal side effects, hypotension
Fluvoxamine[1,2]	Smoking may lower plasma levels	Potential increase in levels with smoking cessation	Moderate	Routine dosage adjustment not recommended, but dosage reduction may be required
Haloperidol[1,2]	Smoking may lower plasma levels Individuals who smoke may required higher dosages	Potential increase in levels with smoking cessation	Moderate	Dosage adjustments may be required Monitor for increased drowsiness, hypotension, and extrapyramidal side effects
Heparin[1,2]	Due to pharmacokinetic and pharmacodynamic drug interactions, individuals who smoke may require increased dosages	Prothrombin time may increase with smoking cessation which can increase the risk of bleeding	Moderate	Close monitoring is required along with potential dosage adjustment according to prothrombin time
Insulin, subcutaneous[1,2,3]	Individuals who smoke may have increased insulin resistance and may require higher dosages	Insulin resistance may decrease with smoking cessation	Moderate	Potential for hypoglycemia - more frequent blood glucose monitoring is recommended Dosage decreases may be required
Irinotecan[1]	Due to multiple pharmacokinetic mechanisms, systemic exposure and efficacy may be reduced with smoking	Potential increase in levels with smoking cessation; however, dosages are not usually adjusted in presence of smoking	Low	Generally no adjustment is required with smoking cessation

Drug	Effect of smoking	Change with Smoking Cessation	Clinical Significance*	Action
Lithium[2]	Smoking increases clearance of caffeine, which indirectly affects lithium levels	Changes in amount of caffeine may affect serum lithium levels (caffeine increases lithium excretion) Theoretically, smoking cessation could indirectly change lithium excretion in the absence of a reduction in caffeine intake	Low	Lithium levels should be checked in patients who havea clinical deterioration
Methadone[2,5]	Methadone is metabolized by multiple enzymes Smoking may increase methadone metabolism	Potential reduction in metabolism with smoking cessation	Moderate	Monitor for signs of methadone toxicity (sedation and respiratory depression) and make dose adjustments accordingly
Mexiletine[1]	Smoking may increase clearance	Potential increase in levels with smoking cessation	Low to Moderate	Monitor for adverse effects
Mirtazepine[2]	Smoking lowers levels	Potential increase in levels with smoking cessation	Low	Monitor for adverse effects and the need for dosage adjustment
Nintedanib[1]	Exposure is reduced by smoking but dosage adjustment is not recommended	Potential increase in level with smoking cessation; however, dosages are not usually adjusted in presence of smoking	Uncategorized	Patients should be advised not to smoke while using nintedanib
Olanzapine[1,2]	Metabolism and clearance increased by smoking Dosage modifications are not routinely recommended but individuals who smoke may require higher dosages	Potential increase in levels with smoking cessation	Moderate to High	Monitor for adverse effects (e.g., dizziness, sedation, hypotension) Dosage reductions may be required
Opioids[1] (pentazocine, dextropopoxyphene)	Smoking may increase the metabolism of some opioids (i.e. propoxyphene and pentazocine) Smoking may decrease the analgesic effect of opioids	Adequate pain control may be experienced with lower opioid doses	Low	Monitor for adverse effects
Pirfenidone[1]	Metabolism increased by smoking	Decreased exposure in individuals who smoke might alter efficacy profile	More Clinically Significant[1]	Patients should be encouraged to stop smoking before and during treatment with pirfenidone
Propranolol[1,3]	Clearance is increased by smoking	Serum levels may rise and effects enhanced	Low to Moderate	May need lower dose
Quinine[2]	Clearance is increased by smoking	Plasma levels may rise with smoking cessation	Low	Monitor for signs of quinine toxicity (e.g. nausea, tremor, tinnitus, visual disturbance) If toxicity occurs, stop the drug and monitor the patient closely
Riociguat[5]	Smoking may reduce exposure to riociguat	Potential for increase in levels with smoking cessation	High	Patients should be advised to quit smoking
Ropinirole[1,2]	Smoking may increase metabolism	Potential for increase in levels with smoking cessation	Low	Monitor for increased adverse effects of ropinirole (e.g. nausea, dizziness) Dosage reduction may be required
Tacrine[1,2]	Smoking may increase metabolism Individuals who smoke may require higher dosages	Potential for increase in levels with smoking cessation	Low	Monitor for adverse effects of tacrine (e.g. gastrointestinal effects, hepatotoxicity) Dosage reduction may be required
Theophylline[1,2]	Smoking increases metabolism Maintenance doses are considerably higher in individuals who smoke	Plasma levels rise with smoking cessation	High	Levels should be monitored if smoking is initiated, discontinued, or changed Dosage adjustment required according to levels
Tricyclic Antidepressants[1] (e.g., imipramine, nortriptyline)	Smoking may decrease blood levels	Serum levels may increase	High	Monitor for side effects and consider dose adjustment if appropriate
Tizanidine[1]	Males who smoke may have lower blood levels	Plasma levels may rise with smoking cessation	Uncategorized	Monitor for adverse effects with smoking cessation
Warfarin[1,2]	Smoking may decrease the serum concentration of warfarin	INR may increase with smoking cessation	Moderate	Monitor the INR more closely and monitor for signs of increased warfarin effect (e.g., bleeding) Advise primary care provider or individual monitoring warfarin of the quit attempt
Zolpidem[2]	Smoking may lower plasma levels and reduce hypnotic effect Individuals who smoke heavily may need higher dosages	Plasma levels may rise with smoking cessation	Moderate	Monitor for increased sedation Dose reduction may be required

*The ratings of clinical significance were taken from the cited sources, which varied in definition and severity. A range of ratings have been presented when there was disagreement across citations.

The content of this document was current at the time of the review. It may not represent a comprehensive list of all potential drug interactions with tobacco smoke, however, given the volume of drug interactions. Assessment and dosage adjustment must be individualized to the specific patient. Professional judgment must be used in applying the information contained in this document.

1. Drug Interactions with Tobacco Smoke, Rx for Change, 2019. https://smokingcessationleadership.ucsf.edu/factsheets/drug-interactions-tobacco-smoke-rx-change-2019.
2. Medication interactions with smoking and smoking cessation. New South Wales Government Health. https://www.health.nsw.gov.au/tobacco/publications/tool-14-medication-intera.pdf
3. Quick guide to drug interactions with smoking cessation. New South Wales Government Health. https://www.health.nsw.gov.au/tobacco/Factsheets/tool-7-guide-dug-interactions.pdf
4. Roche Canada. Tarceva Product Monograph. https://www.rochecanada.com/PMs/Tarceva/Tarceva_PM_E.pdf
5. NHS. What are the clinically significant drug interactions with tobacco smoking? https://www.sps.nhs.uk/wp-content/uploads/2020/03/UKMi_QA_Interactions-with-tobacco_update_Jul-2020.pdf

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