



DRUG INTERACTIONS WITH SMOKING

Many interactions between tobacco smoke and medications have been identified. Tobacco smoke may interact with medications through pharmacokinetic or pharmacodynamic mechanisms. Pharmacokinetic interactions affect the absorption, distribution, metabolism, or elimination of other drugs, potentially causing an altered pharmacologic response. The majority of pharmacokinetic interactions are the result of induction of hepatic cytochrome P450 enzymes (primarily CYP1A2). Pharmacodynamic interactions alter the expected response or actions of other drugs. The most clinically significant interactions are depicted the shaded areas of the table.

DRUG/CLASS	MECHANISM OF INTERACTION AND EFFECTS
Benzodiazepines (diazepam, chlordiazepoxide)	<ul style="list-style-type: none"> ▪ Pharmacodynamic interaction: decreased sedation and drowsiness. ▪ May be caused by central nervous system stimulation by nicotine.
Beta-blockers	<ul style="list-style-type: none"> ▪ Pharmacodynamic interaction: less effective antihypertensive and rate control effects. ▪ May be caused by nicotine-mediated sympathetic activation.
Caffeine	<ul style="list-style-type: none"> ▪ Increased metabolism (induction of CYP1A2); clearance increased by 56%. ▪ Caffeine levels may increase after cessation.
Chlorpromazine (Thorazine)	<ul style="list-style-type: none"> ▪ Decreased area under the curve (AUC) (36%) and serum concentrations (24%). ▪ Smokers may experience less sedation and hypotension and require higher dosages than nonsmokers.
Clozapine (Clozaril)	<ul style="list-style-type: none"> ▪ Increased metabolism (induction of CYP1A2); plasma concentrations decreased by 28%.
Flecainide (Tambocor)	<ul style="list-style-type: none"> ▪ Clearance increased by 61%; trough serum concentrations decreased by 25%. ▪ Smokers may require higher dosages.
Fluvoxamine (Luvox)	<ul style="list-style-type: none"> ▪ Increased metabolism (induction of CYP1A2); clearance increased by 25%; decreased plasma concentrations (47%). ▪ Dosage modifications not routinely recommended but smokers may require higher dosages.
Haloperidol (Haldol)	<ul style="list-style-type: none"> ▪ Clearance increased by 44%; serum concentrations decreased by 70%.
Heparin	<ul style="list-style-type: none"> ▪ Mechanism unknown but increased clearance and decreased half-life are observed. ▪ Smokers may require higher dosages.
Insulin	<ul style="list-style-type: none"> ▪ Insulin absorption may be decreased secondary to peripheral vasoconstriction; smoking may cause release of endogenous substances that antagonize the effects of insulin. ▪ Smokers may require higher dosages.
Mexiletine (Mexitil)	<ul style="list-style-type: none"> ▪ Clearance (via oxidation and glucuronidation) increased by 25%; half-life decreased by 36%.
Olanzapine (Zyprexa)	<ul style="list-style-type: none"> ▪ Increased metabolism (induction of CYP1A2); clearance increased by 40–98%. ▪ Dosage modifications not routinely recommended but smokers may require higher dosages.
Opioids (propoxyphene, pentazocine)	<ul style="list-style-type: none"> ▪ Pharmacodynamic interaction: decreased analgesic effect; higher dosages necessary in smokers. ▪ Mechanism unknown.
Propranolol (Inderal)	<ul style="list-style-type: none"> ▪ Clearance (via side chain oxidation and glucuronidation) increased by 77%.
Oral contraceptives	<ul style="list-style-type: none"> ▪ Pharmacodynamic interaction: increased risk of cardiovascular adverse effects (e.g., stroke, myocardial infarction, thromboembolism) in women who smoke and use oral contraceptives. ▪ Risk increases with age and with heavy smoking (15 or more cigarettes per day) and is quite marked in women over age 35 years.
Tacrine (Cognex)	<ul style="list-style-type: none"> ▪ Increased metabolism (induction of CYP1A2); half-life decreased by 50%; serum concentrations threefold lower. ▪ Smokers may require higher dosages.
Theophylline (Theo Dur, etc)	<ul style="list-style-type: none"> ▪ Increased metabolism (induction of CYP1A2); clearance increased by 58–100%; half-life decreased by 63%. ▪ Theophylline levels should be monitored if smoking is initiated, discontinued, or changed. ▪ Maintenance doses are considerably higher in smokers.

Adapted from Zevin S, Benowitz NL. Drug interactions with tobacco smoking. *Clin Pharmacokinet* 1999;36:425–438.