

Cytochrome P450 Drug Interactions Table

Use of this Table:

- Definitions
Substrates: drugs that are metabolized as substrates by the enzyme
Inhibitors: drugs that prevent the enzyme from metabolizing the substrates
Activators: drugs that increase the enzyme's ability to metabolize the substrates
- The table contains lists of drugs in columns under the designation of specific cytochrome P450 isoforms. A drug appears in a column if there is published evidence that it is metabolized, at least in part, via that isoform. It does not necessarily follow that the isoform is the principal metabolic pathway *in vivo*, or that alterations in the rate of the metabolic reaction catalyzed by that isoform will have large effects on the pharmacokinetics of the drug.
- This P450 table was taken from the website <http://medicine.iupui.edu/flockhart/> and is maintained by David A. Flockhart, MD, PhD, in the Division of Clinical Pharmacology at Indiana University School of Medicine. This table is intended to be used as an educational tool. For specific literature references to drugs in this table, please refer to Website <http://medicine.iupui.edu/flockhart/>.

The information was obtained from the above website on July 19, 2004. This web page is updated as new information becomes available.

Substrates

1A2	2B6	2C8	2C19	2C9	2D6	2E1	3A4,5,7
amitriptyline caffeine clomipramine clozapine cyclobenzaprine (Flexeril®) estradiol flovoxamine haloperidol imipramineN-DeMe mexiletine naproxen olanzapine ondansetron phenacetin=>acetaminophen =>NAPQI propranolol riluzole ropivacaine tacrine theophylline verapamil (R)warfarin zileuton zolmitriptan	bupropion cyclophosphamide efavirenz ifosfamide methadone	paclitaxel torsemide amodiaquine cerivastatin repaglinide	Proton Pump Inhibitors: omeprazole lansoprazole pantoprazole E-3810	NSAIDs: diclofenac ibuprofen meloxicam S-naproxen=>Nor piroxicam suprofen	Beta Blockers: carvedilol S-metoprolol propafenone timolol	Anesthetics: enflurane halothane isoflurane methoxyflurane sevoflurane	Macrolide Antibiotics: clarithromycin erythromycin (not 3A5) NOT azithromycin Anti-arrhythmics: quinidine=>3-OH (not 3A5)
			Oral Hypoglycemic Agents: tolbutamide glipizide	Antidepressants: amitriptyline clomipramine desipramine imipramine paroxetine	Benzodiazepines: alprazolam diazepam=>3OH midazolam triazolam		
			Anti-epileptics: diazepam=>Nor phenytoin(O) S-mephenytoin phenobarbitone	Angiotensin II Blockers: irbesartan losartan Sulfonylureas: Glyburide Glibenclamide Glipizide Glimepiride tolbutamide	Antipsychotics: haloperidol perphanazine risperidone=>9OH thioridazine		Acetaminophen =>NAPQI aniline benzene chlorzoxazone ethanol N,N-dimethyl Formamide theophylline=>8-OH
amiptriptyline carisoprodol citalopram clomipramine cyclophosphamide hexobarbital imipramine N-DeMe indomethacin R-mephobarbital moclobemide nelfinavir nilutamide primidone progesterone proguanil propranolol teniposide R-warfarin=>8-OH	amitriptyline celecoxib fluoxetine fluvastatin glyburide nateglinide phenytoin=>4-OH rosiglitazone tamoxifen torsemide S-warfarin	alprenolol amphetamine atomoxetine bufuralol chlorpheniramine chlorpromazine codeine (=>O-desMe) debrisoquine dexfenfluramine dextromethorphan ecainide flecainide fluoxetine fluvoxamine lidocaine metoclopramide methoxyamphetamine mexiletine nortriptyline minaprine ondansetron perhexiline	HIV Antivirals: indinavir nelfinavir ritonavir saquinavir Prokinetic: cisapride Antihistamines: astemizole chlorpheniramine terfenidine Calcium Channel Blockers: amlodipine diltiazem felodipine lercanidipine nifedipine nisoldipine nitrendipine verapamil				

Substrates Continued

1A2	2B6	2C8	2C19	2C9	2D6	2E1	3A4,5,7
					phenacetin phenformin propranolol(=>4OH) sparteine tamoxifen tramadol venlafaxine		HMG CoA Reductase Inhibitors atorvastatin cerivastatin lovastatin NOT pravastatin simvastatin
							Steroid 6beta-OH estradiol hydrocortisone progesterone testosterone
							Miscellaneous alfentanyl buspirone cafergot caffiene=>TMU cocaine dapson codeine-N demethylation dextromethophan eplerenone fentanyl finasteride gleevec haloperidol irinotecan LAAM lidocaine methadone nateglinide odanestron pimozide propranolol quinie Not rosuvastatin salmeterol sildenafil sirolimus tamoxifen taxol terfenadine trazodone vincristine zaleplon zolpidem

Inhibitors

1A2	2B6	2C8	2C19	2C9	2D6	2E1	3A4,5,7
amiodarone cimetidine fluoroquinolones fluvoxamine furafylline interferon? methoxsalen mibefradil ticlopidine	thiotepa	trimethoprim quercetin glitazones gemfibrozil	cimetidine felbamate fluoxetine fluvoxamine indomethacin ketoconazole lansoprazole modafinil omeprazole paroxetine probenicid ticlopidine topiramate	amiodarone fluconazole fluvastatin fluvoxamine isoniazid lovastatin paroxetine phenylbutazone probenicid sertraline sulfamethoxazole sulfaphenazole teniposide trimethoprim zafirlukast	amiodarone bupropion celecoxib chlorpromazine chlorpheniramine cimetidine clomipramine cocaine doxorubicin fluoxetine halofantrine red-haloperidol levomepromazine metoclopramide methadone mibefradil moclobemide paroxetine quinidine ranitidine ritonavir sertraline terbinafine histamine H1 receptor antagonists diphenhydramine chlorpheniramine demastine perphenazine hydroxyzine tripeleennamine	diethyl-dithiocarbamate disulfiram	HIV Antivirals: delaviridine indinavir nelfinavir ritonavir saquinavir amiodarone NOT azithromycin chloramphenicol cimetidine ciprofloxacin clarithromycin diethyl-dithiocarbamate diltiazem erythromycin fluconazole fluvoxamine gestodene grapefruit juice itraconazole ketoconazole mifepristone nefazodone norfloxacin norfluoxetine mibefradil star fruit verapamil

Inducers

1A2	2B6	2C8	2C19	2C9	2D6	2E1	3A4,5,7
broccoli brussel sprouts char-grilled meat insulin methly cholanthrene modafinil nafcillin? beta- naphthoflavone omeprazole tobacco	phenobarbital rifampin	rifampin	carbamazepine norethindrone NOT pentobarbital prednisone rifampin	rifampin secobarbital	dexamethasone rifampin?	ethanol isoniazid	HIV Antivirals: efavirenz nevirapine barbiturates carbamazepine glucocorticoids modafinil phenobarbital phenytoin rifampin St. John's wort troglitazone pioglitazone rifabutin

Administration Schedule for Antidepressants

Antidepressants	Therapeutic Dose Range (mg/day)	Initial Suggested Dose	Administration Schedule**
Selective Serotonin Reuptake Inhibitors (SSRIs)¹			
Citalopram (Celexa)	10 - 40	20 mg in morning with food (10 mg in elderly and those with comorbid panic disorder)	Increase in 10 mg increments every 7 days as tolerated. Maintain 20 mg for 4 weeks before dose increase.
Fluoxetine (Prozac)	10 - 40	20 mg in morning with food (10 mg in elderly and those with comorbid panic disorder)	Increase in 10 mg increments at intervals of 7 days. Maintain 20 mg for 4-6 weeks before dose increase. If significant side effects occur within 7 days, lower dose or change medication.
Fluvoxamine (Luvox)	50 - 300	=100 mg in morning with food (50 mg in elderly and those with comorbid panic disorder)	Increase in 50 mg increments every 7 days as tolerated. Maintain 200 mg for at least 4 weeks before further dose increase.
Paroxetine (Paxil)	10 - 50	20 mg once daily, usually in morning with food (10mg in elderly and those with comorbid panic disorder)	Increase in 10 mg increments at intervals of approximately 7 days up to a maximum of 40 mg/day. Maintain 20 mg for 4 weeks before dose increase.
Sertraline (Zoloft)	50 - 150	50 mg once daily, usually in morning with food	Increase in 50 mg increments at intervals of 7 days as tolerated. Maintain 100 mg for 4 weeks before dose increase.
Newer / Atypical Antidepressants			
Bupropion ² (Wellbutrin SR)	150 - 450	100 mg in morning	Increase to 100 mg twice/day after 7 days. Then increase to 150 mg twice/day after 3 weeks and to 150 mg three times daily after 6 weeks.
Mirtazapine (Remeron)	15 - 45	15 mg at bedtime (7.5 mg in elderly and those with comorbid panic disorder)	Increase in 15 mg increments (7.5 mg in elderly) as tolerated. Maintain 30 mg for 4 weeks before further dose increase.
Nefazodone ³ (Serzone)	200 - 600	100 mg twice a day with food	Increase in 100 mg increments at intervals of 7 days as tolerated. Administer in divided doses. Maintain 200 mg twice/day for 4 weeks before dose increase.
Venlafaxine ⁴ (Effexor XR)	75 - 300	37.5 mg in morning with food	Increase to 75 mg in morning after 1 week, 150 mg in the morning after 2 weeks, 225 mg in the morning after 4 weeks, and 300 mg in the morning after 6 weeks.
Tricyclic Antidepressants (TCAs)⁵			
Desipramine (Norpramin)	75 - 300	50 mg at bedtime (25 mg in elderly)	Increase in 25 mg increments every 7 days as tolerated to full therapeutic dose over period of several weeks. Once daily dosing at bedtime often minimizes side effects. Adequate trial considered to be 150 mg/day for at least 4 weeks.
Doxepin (Sinequan)	75 - 300	50 mg at bedtime (25 mg in elderly)	Increase in 25 mg increments every 7 days as tolerated to full therapeutic dose over period of several weeks. Once daily dosing at bedtime often minimizes side effects. Adequate trial considered to be 150 mg/day for at least 4 weeks.
Imipramine (Tofranil)	75 - 300	50 mg at bedtime	Increase in 25 mg increments every 7 days as tolerated to full therapeutic dose over period of several weeks. Once daily dosing at bedtime often minimizes side effects. Adequate trial considered to be 150 mg/day for at least 4 weeks.
Nortriptyline (Pamelor)	40 - 200	25 mg (10 mg in elderly)	Increase in 10-25 mg increments every 7 days as tolerated to full therapeutic dose over period of several weeks. Only TCA with therapeutic window. Dosing too high may be ineffective. Suggest obtaining serum drug levels ⁶ after 4 weeks if not effective.

GENERAL NOTES ABOUT PRESCRIBING ANTIDEPRESSANTS

1. Many antidepressants are contraindicated for use in conjunction with monoamine oxidase inhibitors (MAOIs). Consultation with a psychiatrist or pharmacist is recommended before co-administering MAOIs and other antidepressant medications.
2. Consultation with a psychiatrist is recommended before prescribing antidepressants to pregnant females.
3. CAUTIONARY NOTE REGARDING USE OF ANTIDEPRESSANTS IN PATIENTS WITH PARKINSON'S DISEASE: Treatment of Parkinson's disease often includes the use of selegiline HCl (Eldepryl), which is a type B monoamine oxidase inhibitor (MAOI). Because the use of many antidepressants is contraindicated in conjunction with an MAOI as stated above, the discontinuation of Eldepryl in order to use certain antidepressants may be warranted.

** Doses should be increased as tolerated and as clinically indicated. Many patients will respond at doses below the maximum doses indicated in the therapeutic dose range.

¹ SSRIs are recommended in depressed patients with comorbid panic or obsessive-compulsive disorder.

² Avoid bupropion in patients at high risk for seizures such as patients with a history of seizures, significant central nervous system lesions, or head trauma. Also avoid bupropion in depressed patients with significant comorbid anxiety or bulimia.

³ Do not combine nefazodone (Serzone) with other drugs that are extensively metabolized by the P450 3A4 isoenzyme system such as terfenadine, astemizole and cisapride.

⁴ Venlafaxine (Effexor XR) can cause increases in blood pressure at higher doses.

⁵ Tricyclics (TCAs) have lower costs but may have more adverse side effects than SSRIs and other newer antidepressants. TCAs may be contraindicated in patients with certain physical comorbidities such as recent myocardial infarction, cardiac conduction defects, urinary retention, narrow angle glaucoma, orthostatic hypotension, renal failure and delirium / acute confusional states. Tertiary amine TCAs such as doxepin (Sinequan), imipramine (Tofranil) and amitriptyline (Elavil) are not recommended in older adults due to their unfavorable side effect profiles.

⁶ Target blood level is 50-150 ng/mL.

10. Rost K. The Depression Tool Kit for Primary Care (Prototype).



Physician Antidepressant Fact Sheet

Extended Use of Minor Tranquilizers to Treat Depression Is Contraindicated ⁽¹⁰⁾ Anxiolytic medications (benzodiazepines and barbiturates) have not been shown to be effective in treating depression. Anxiolytics may be useful in special cases as an adjunctive medication (not to exceed 12 weeks) for patients with pronounced anxiety. Benzodiazepines may be useful (not to exceed 6 weeks) for pronounced insomnia. **Treating Elderly Patients With Antidepressants (10)** ⁽¹⁰⁾ More sensitive to side effects, particularly to those of tricyclics; start with SSRIs, consider using secondary amine tricyclics (e.g., nortriptyline, desipramine) if nonresponsive to SSRIs. Are often on multiple other medications (beware of drug interactions). Metabolism is slower; start with lower doses, increase doses slowly. **Discontinuing Antidepressant Therapy** ⁽¹⁰⁾

While antidepressant medications are generally considered safe, they should be discontinued if they are not required. For first episodes of depression, it may be appropriate to discontinue medication after 4-9 months of continuation phase treatment since only 50% will have another episode of depression. Tricyclic antidepressants and other drugs listed on the administration schedule should be tapered if the patient has had exposure at therapeutic dosages for 3 months or more. A tapering schedule of tricyclics over 2 to 4 weeks is recommended.

This Administration Schedule for Antidepressants was taken from the MacArthur Tool Kit, Allan J. Dietrich, MD, Head, MacArthur Initiative Steering Committee, Dartmouth Medical School.

=Please note per Drug Facts and Comparisons, 2002, Luvox starting dose is 50mg as a single daily bedtime dose. The dose should be increased in 50mg increments every 4-7 days, as tolerated until maximum therapeutic benefit is achieved and not to exceed 300mg/day. Anything greater than 100mg should be in two divided doses.

This chart is intended to be used as an educational tool and should not replace clinical judgement.