

Flockhart Table™

“The effective, intelligent management of many problems related to drug interactions in clinical prescribing can be helped by an understanding of how drugs are metabolized. Specifically, if a prescriber is aware of the dominant cytochrome P450 isoform involved in a drug's metabolism, it is possible to anticipate, from the inhibitor and inducer lists for that enzyme, which drugs might cause significant interactions.”

- 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

Taken from: <http://medicine.iupui.edu/CLINPHARM/ddis/pocket-card>

Furthermore, Pocket Cards can be ordered from: <http://medicine.iupui.edu/CLINPHARM/ddis/pocket-card>

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P450 Drug Interaction Table

SUBSTRATES drugs that are metabolized as substrates by the enzyme

| 1A2 | 2B6 | 2C8 | 2C9 | 2C19 | 2D6 | 2E1 | 3A4,5,7 |
|---------------------------|------------------------|--------------|--------------------------|----------------------------|-------------------------|----------------------------|---------------------------|
| amitriptyline | artemisinin | amodiaquine | NSAIDs: | PPIs: | tamoxifen: | Anesthetics: | Macrolide |
| caffeine ₂ | bupropion ₁ | ² | diclofenac ¹ | esomeprazole | TAMOXIFEN | enflurane | antibiotics: |
| clomipramine | cyclophosphamid | cerivastatin | ibuprofen | lansoprazole | GUIDE | halothane | clarithromycin |
| clozapine | e | paclitaxel | lornoxiam | omeprazole ₂ | Beta Blockers: | isoflurane | erythromycin ² |
| cyclobenzaprine | efavirenz ₁ | repaglinide | meloxicam | pantoprazole | carvedilol | methoxyflurane | (not 3A5) |
| duloxetine | ifosphamide | sorafenib | S- | | S-metoprolol | sevoflurane | NOT |
| estradiol | ketamine | torseמיד | naproxen→Nor | Anti-epileptics: | propafenone | | azithromycin |
| fluvoxamine | mepidine | | piroxicam | diazepam→Nor | timolol | acetaminophen→NAP | telithromycin |
| haloperidol | methadone | | suprofen | phenytoin(O) | | QI | |
| imipramine N-DeMe | nevirapine | | | S-mephenytoin ¹ | Antidepressants: | aniline ₂ | Anti- |
| mexiletine | propafol | | Oral | phenobarbitone | amitriptyline | benzene | arrhythmics: |
| nabumetone | selegiline | | Hypoglycemic | | clomipramine | chlorzoxazone ₁ | quinidine→3-OH |
| naproxen | sorafenib | | Agents: | amitriptyline | desipramine | ethanol | (not 3A5) |
| olanzapine | | | tolbutamide ¹ | carisoprodol | fluoxetine | N,N- | |
| ondansetron | | | glipizide | citalopram | imipramine | dimethylformamide | Benzodiazepines |
| phenacetin ₁ → | | | | chloramphenicol | | theophylline→8-OH | : |
| acetaminophen | | | | | | | |

Substrates continued

| 1A2 | 2B6 | 2C8 | 2C9 | 2C19 | 2D6 | 2E1 | 3A4,5,7 |
|---------------------------|-----|-----|---------------------------------|---------------------|-------------------------------|-----|----------------------------------|
| →NAPQI | | | Angiotensin II Blockers: | clomipramine | paroxetine | | alprazolam |
| propranolol | | | losartan | clopidogrel | venlafaxine | | diazepam→3OH |
| riluzole | | | irbesartan | cyclophosphamid | | | midazolam ¹ |
| ropivacaine | | | | e | Antipsychotics: | | triazolam ² |
| tacrine ₂ | | | Sulfonylureas: | hexobarbital | haloperidol | | |
| theophylline ₂ | | | glyburide | imipramine N-DeME | perphenazine | | Immune Modulators: |
| tizanidine | | | glibenclamide | indomethacin | risperidone→9-OH | | cyclosporine |
| triamterene | | | glipizide | labetalol | thioridazine | | tacrolimus |
| verapamil | | | glimepiride | R-mephobarbital | zuclopenthixol | | (FK506) |
| (R)warfarin | | | tolbutamide | moclobemide | alprenolol | | |
| zileuton | | | | nelfinavir | amphetamine | | HIV Antivirals: |
| zolmitriptan | | | amitriptyline | nilutamide | aripiprazole | | indinavir |
| | | | celecoxib | primidone | atomoxetine | | nelfinavir |
| | | | fluoxetine | progesterone | bufuralol ¹ | | ritonavir |
| | | | fluvastatin | proguanil | chlorpheniramine | | saquinavir |
| | | | glyburide | propranolol | chlorpromazine | | |
| | | | nateglinide | teniposide | clonidine | | Prokinetic: |
| | | | phenytoin-4-OH ₂ | R-warfarin→8-OH | codeine (→O-desMe) | | cisapride |
| | | | rosiglitazone | <u>voriconazole</u> | debrisoquine ² | | Antihistamines: |
| | | | tamoxifen | | dexfenfluramine | | astemizole |
| | | | toremide | | dextromethorphan ¹ | | chlorpheniramine |
| | | | valproic acid | | donepezil | | terfenadine ² |
| | | | S-warfarin ¹ | | duloxetine | | |
| | | | <u>zakirlukast</u> | | encainide | | Calcium Channel Blockers: |
| | | | | | flecainide | | amlodipine |
| | | | | | fluvoxamine | | diltiazem |
| | | | | | lidocaine | | felodipine |
| | | | | | metoclopramide | | lercanidipine |
| | | | | | methoxyamphetami | | nifedipine ² |
| | | | | | ne | | |
| | | | | | mexiletine | | |

Substrates continued

| 1A2 | 2B6 | 2C8 | 2C9 | 2C19 | 2D6 | 2E1 | 3A4,5,7 |
|-----|-----|-----|-----|------|--|-----|--|
| | | | | | minaprine nebivolol nortriptyline ondansetron oxycodone perhexiline phenacetin phenformin promethazine propafenone propranolol risperidone sparteine tramadol | | nisoldipine nitrendipine verapamil |
| | | | | | | | HMG CoA Reductase Inhibitors: atorvastatin cerivastatin lovastatin NOT pravastatin NOT rosuvastatin simvastatin |
| | | | | | | | Steroid 6beta-OH: estradiol hydrocortisone progesterone testosterone ¹ |
| | | | | | | | Miscellaneous: alfentanil aprepitant aripiprazole boceprevir buspirone carbamazepine cafergot caffeine→TMU cilostazol cocaine codeine-N- |

Substrates continued

| 1A2 | 2B6 | 2C8 | 2C9 | 2C19 | 2D6 | 2E1 | 3A4,5,7 |
|-----|-----|-----|-----|------|-----|-----|-----------------------------------|
| | | | | | | | demethylation |
| | | | | | | | dapsone |
| | | | | | | | dexamethasone |
| | | | | | | | dextromethorpha n ² |
| | | | | | | | docetaxel |
| | | | | | | | domperidone |
| | | | | | | | eplerenone |
| | | | | | | | fentanyl |
| | | | | | | | finasteride |
| | | | | | | | gleevec |
| | | | | | | | haloperidol |
| | | | | | | | irinotecan |
| | | | | | | | LAAM |
| | | | | | | | lidocaine |
| | | | | | | | methadone |
| | | | | | | | nateglinide |
| | | | | | | | nevirapine |
| | | | | | | | ondansetron |
| | | | | | | | pimozide |
| | | | | | | | propranolol |
| | | | | | | | quetiapine |
| | | | | | | | quinine |
| | | | | | | | risperidone |
| | | | | | | | romidepsin |
| | | | | | | | salmeterol |
| | | | | | | | sildenafil |
| | | | | | | | sirolimus |
| | | | | | | | sorafenib |
| | | | | | | | sunitinib |
| | | | | | | | tamoxifen |
| | | | | | | | taxol |
| | | | | | | | telaprevir |

Substrates continued

| | | | | | | | |
|-----|-----|-----|-----|------|-----|-----|--|
| 1A2 | 2B6 | 2C8 | 2C9 | 2C19 | 2D6 | 2E1 | 3A4,5,7 |
| | | | | | | | terfenadine torisel trazodone vemurafenib vincristine zaleplon ziprasidone zolpidem |

INHIBITORS drugs that prevent the enzyme from metabolizing the substrates

Inhibitors compete with other drugs for a particular enzyme thus affecting the optimal level of metabolism of the substrate drug which in many cases affect the individual's response to that particular medication, e.g. making it ineffective.

■ **A Strong inhibitor** is one that causes a > 5-fold increase in the plasma AUC values or more than 80% decrease in clearance.

■ **A Moderate inhibitor** is one that causes a > 2-fold increase in the plasma AUC values or 50-80% decrease in clearance.

■ **A Weak inhibitor** is one that causes a > 1.25-fold but < 2-fold increase in the plasma AUC values or 20-50% decrease in clearance.

FDA preferred¹ and acceptable² **inhibitors** for in vitro experiments.*

| 1A2 | 2B6 | 2C8 | 2C9 | 2C19 | 2D6 | 2E1 | 3A4,5,7 |
|--|---|---|--|--|--|--|--|
| ■ fluvoxamine ■ ciprofloxacin ■ cimetidine | clopidogrel thiotepa ticlopidine ² voriconazole | ■ gemfibrozil ² ■ trimethoprim ² | ■ fluconazole ² ■ amiodarone efavirenz fenofibrate glitazones montelukast ¹ quercetin ¹ | PPIs: esomeprazole lansoprazole omeprazole ² pantoprazole | ■ bupropion ■ cinacalcet ■ fluoxetine ■ paroxetine ■ quinidine ¹ ■ duloxetine ■ sertraline ■ terbinafine | diethyl- dithiocarbamate ² disulfiram | HIV Antivirals: ■ indinavir ■ nelfinavir ■ ritonavir ■ clarithromycin ■ itraconazole ¹ ■ ketoconazole ■ nefazodone ■ saquinavir |
| amiodarone efavirenz fluoroquinolones fluvoxamine furafylline ¹ | | | fluvastatin fluvoxamine ² isoniazid | Other: chloramphenicol | | | |

| 1A2 | 2B6 | 2C8 | 2C9 | 2C19 | 2D6 | 2E1 | 3A4,5,7 |
|-----|-----|-----|-----|------|-----|-----|---------|
|-----|-----|-----|-----|------|-----|-----|---------|

INDUCERS drugs that increase the enzyme's ability to metabolize the substrates

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

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