



### Cytochrome P450 Drug Metabolism/Inhibition

For a complete list see: <http://medicine.iupui.edu/clinpharm/ddis/>

Adapted from Indiana University Department of Medicine Division of Clinical Pharmacology website.

#### 1A2

Substrates	Significant enzyme inducers	*Significant enzyme inhibitors
<u>Clinically Relevant</u> Clozapine Cyclobenzaprine Duloxetine Fluvoxamine Haloperidol Imipramine Mexiletine Nabumetone Naproxen Olanzapine Riluzole Tacrine Theophylline Tizanidine Triamterene Zileuton Zolmitriptan	<u>Clinically Relevant</u> Carbamazepine Chargrilled meat Rifampin Tobacco	<u>Clinically Relevant</u> Amiodarone Cimetidine (weak) Efavirenz Fluoroquinolones Fluvoxamine (strong) Ticlopidine

#### 2B6

Substrates	Significant enzyme inducers	*Significant enzyme inhibitors
<u>Clinically Relevant</u> Artemisinin Bupropion Cyclophosphamide Efavirenz Ifosfamide Ketamine Meperidine Methadone Nevirapine Propofol Selegiline	<u>Clinically Relevant</u> Artemisinin Carbamazepine Efavirenz Nevirapine Phenobarbital Phenytoin Rifampin	<u>Clinically Relevant</u> Clopidogrel Thiotepa Ticlopidine Voriconazole

#### 2C8

Substrates	Significant enzyme inducers	*Significant enzyme inhibitors
<u>Clinically Relevant</u> Amodiaquine Cerivastatin Paclitaxel Repaglinide Torseamide	<u>Clinically Relevant</u> None listed.	<u>Clinically Relevant</u> Gemfibrozil (strong) Montelukast

## 2C9

<b>Substrates</b>	<b>Significant enzyme inducers</b>	<b>*Significant enzyme inhibitors</b>
<u>Clinically Relevant</u> <b>NSAIDs</b> Celecoxib Diclofenac Ibuprofen Naproxen Piroxicam  <b>Oral Hypoglycemics</b> Glipizide Glyburide Rosiglitazone Tolbutamide  <b>Angiotensin II Blockers</b> Irbesartan Losartan  <b>Others</b> Fluvastatin Phenytoin Torsemide Valproic acid Warfarin Zafirlukast	<u>Clinically Relevant</u> Carbamazepine Nevirapine Phenobarbital Rifampin St. John's Wort	<u>Clinically Relevant</u> Amiodarone (moderate) Efavirenz Fluconazole (strong) Isoniazid Metronidazole Paroxetine Sulfamethoxazole Voriconazole

## 2C19

<b>Substrates</b>	<b>Significant enzyme inducers</b>	<b>*Significant enzyme inhibitors</b>
<u>Clinically Relevant</u> <b>PPIs</b> Esomeprazole Lansoprazole Omeprazole Pantoprazole  <b>Anti-epileptics</b> Diazepam Phenobarbitone Phenytoin  <b>Others</b> Amitriptyline Carisoprodol Citalopram Clomipramine Clopidogrel Cyclophosphamide Imipramine Labetalol Proguanil Voriconazole	<u>Clinically Relevant</u> Efavirenz Rifampicin Ritonavir St. John's Wort	<u>Clinically Relevant</u> Cimetidine Esomeprazole Felbamate Fluoxetine Fluvoxamine Isoniazid Ketoconazole Lansoprazole Omeprazole Oral contraceptives Pantoprazole Ticlopidine Voriconazole

## 2D6

Substrates	Significant enzyme inducers	*Significant enzyme inhibitors
<u>Clinically Relevant</u> <b>Beta Blockers</b> Carvedilol S-metoprolol Propafenone Timolol  <b>Antidepressants</b> Amitriptyline Clomipramine Desipramine Doxepin Duloxetine Fluoxetine Imipramine Paroxetine Venlafaxine  <b>Antipsychotics</b> Aripiprazole Haloperidol Risperidone Thioridazine  <b>Others</b> Atomoxetine Codeine Dextromethorphan Flecainide Mexiletine Ondansetron Oxycodone Tamoxifen Tramadol	<u>Clinically Relevant</u> None listed.	<u>Clinically Relevant</u> Bupropion (strong) Fluoxetine (strong) Paroxetine (strong) Quinidine (strong)  Duloxetine (moderate)  Amiodarone (weak) Cimetidine (weak)  Aripiprazole Chlorpheniramine Clomipramine Diphenhydramine Doxepin Haloperidol Methadone Ritonavir Terbinafine (moderate)

## 2E1

Substrates	Significant enzyme inducers	*Significant enzyme inhibitors
<u>Clinically Relevant</u> <b>Anesthetics</b> Enflurane Halothane Isoflurane Methoxyflurane Sevoflurane  <b>Others</b> Acetaminophen →NAPQI Aniline Benzene Chlorzoxazone Ethanol N,N-dimethyl formamide Theophylline→8-OH	<u>Clinically Relevant</u> Ethanol Isoniazid	<u>Clinically Relevant</u> Disulfiram

3A4, 5, 7

Substrates	Significant enzyme inducers	*Significant enzyme inhibitors
<p><u>Clinically Relevant</u>  <b>Macrolide antibiotics</b>            Clarithromycin            Erythromycin (not 3A5)            Telithromycin</p> <p>Not azithromycin</p> <p><b>Anti-arrhythmics</b>            Quinidine→3-OH (not 3A5)</p> <p><b>Benzodiazepines</b>            Alprazolam            Diazepam →3OH            Midazolam            Triazolam</p> <p><b>Immune Modulators</b>            Cyclosporine            Sirolimus            Tacrolimus (FK506)</p> <p><b>HIV Antivirals</b>            Indinavir            Nevirapine            Ritonavir            Saquinavir</p> <p><b>Prokinetics</b>            Cisapride</p> <p><b>Antihistamines</b>            Astemizole            Chlorpheniramine</p> <p><b>Calcium Channel Blockers</b>            Amlodipine            Diltiazem            Felodipine            Nifedipine            Nisoldipine            Nitrendipine            Verapamil</p> <p><b>HMG CoA Reductase Inhibitors</b>            Atorvastatin            Lovastatin            Simvastatin</p> <p>NOT pravastatin            NOT rosuvastatin</p> <p><b>PDE-5 Inhibitors</b>            Sildenafil            Tadalafil</p>	<p><u>Clinically Relevant</u>            Carbamazepine            Efavirenz            Nevirapine            Phenobarbital            Phenytoin            Pioglitazone            Rifabutin            Rifampin            St. John's Wort            Troglitazone</p>	<p><u>Clinically Relevant</u>  <b>HIV Antivirals</b>            Indinavir (strong)            Nelfinavir (strong)            Ritonavir (strong)</p> <p>Clarithromycin (strong)            Itraconazole (strong)            Ketoconazole (strong)            Nefazodone (strong)</p> <p>Diltiazem (moderate)            Erythromycin (moderate)            Grapefruit juice (moderate)            Verapamil (moderate)</p> <p>Cimetidine (weak)</p> <p>Amiodarone            Fluvoxamine            Troleandomycin            Voriconazole</p> <p>Not azithromycin</p>

Vardenafil		
<b>Others</b>		
Alfentanil		
Aripiprazole		
Boceprevir		
Buspirone		
Carbamazepine		
Gleevec		
Haloperidol		
Pimozide		
Quinine		
Tamoxifen		
Telaprevir		
Trazodone		
Vincristine		

**\*Inhibitors**

Strong inhibitor – causes a > 5-fold increase in the plasma AUC values or more than 80% decrease in clearance

Moderate inhibitor – causes a > 2-fold increase in the plasma AUC values or 50-80% decrease in clearance

Weak inhibitor – causes a > 1.25-fold but < 2-fold increase in the plasma AUC values or 20-50% decrease in clearance