

**Major Drug Classes Divided by Known CYP2D6 Inhibitory Activity (from Sideras et al, JCO, 2010;28:2768-76)**

Class	Moderate-to-potent inhibitors with clearly demonstrated or expected in vivo inhibition <sup>†</sup>	Weak-to-moderate inhibitors that have demonstrated or could potentially have some in vivo effect <sup>‡</sup>	Alternative drugs expected to have little in vivo inhibition <sup>§</sup>
SSRI/SNRIs	Paroxetine*	Sertraline*	Venlafaxine*
	Fluoxetine*	Citalopram*	Desvenlafaxine
	Bupropion	Fluvoxamine	Reboxetine
	Duloxetine		Escitalopram Mirtazapine
Tricyclic antidepressants		Clomipramine	
		Doxepin	
		Desipramine	
		Imipramine	
		Amitriptyline	
		Nortriptyline	
Antipsychotics	Thioridazine	Chlorpromazine	Thiothixene
	Perphenazine	Fluphenazine	Clozapine
	Pimozide	Haloperidol	Risperidone Clozapine Olanzapine Ziprasidone Quetiapine
Cardiac medications	Quinidine	Amiodarone	Diltiazem
	Ticlopidine	Nicardipine	
		Verapamil	
		Amlodipine	
		Felodipine	
		Nifedipine	
Medications for infectious diseases	Terbinafine	Ritonavir	Indinavir
	Quinidine <sup>  </sup>	Halofantrine	Saquinavir
		Chloroquine	Nelfinavir
			Delavirdine Nevirapine Efavirenz
H2 blockers		Cimetidine	Ranitidine
H1 blockers <sup>¶</sup>		Clemastine	Chlorpheniramine
		Tripelennamine	Cetirizine
		Promethazine	Loratadine
		Hydroxyzine	
		Diphenylpyraline	
Miscellaneous	Cinacalcet	Celecoxib	Gabapentin

Abbreviations: CYP2D6, cytochrome P450 2D6; SSRI, selective serotonin reuptake inhibitor; SNRI, selective noradrenergic reuptake inhibitor; AUC, area under the concentration-time curve.

<sup>†</sup> Medications with in vivo data that demonstrate an effect on endoxifen concentrations when coprescribed with tamoxifen.

<sup>†</sup> Medications classified as moderate-to-potent inhibitors have demonstrated in vivo inhibition of CYP2D6 substrates with an increase in the plasma AUC of the substrate by at least two-fold or higher and/or in vitro inhibition using human liver microsome systems with in vitro inhibition constant (K<sub>i</sub>) values  $\leq 1$   $\mu\text{mol/L}$ . These medications are expected to have or have demonstrated phenotypic conversion of extensive metabolizers to poor metabolizers and significant reduction in endoxifen levels. They should not be administered to women receiving tamoxifen for prolonged periods of time.

<sup>†</sup> Medications classified as weak-to-moderate inhibitors have demonstrated in vivo inhibition of CYP2D6 substrates with an increase in the plasma AUC of the substrate by less than two-fold and/or in vitro inhibition using human liver microsome systems with K<sub>i</sub> values in the range of 2 to 10  $\mu\text{mol/L}$ . Although these medications have either demonstrated lesser reductions in endoxifen levels, or could potentially result in reduction of endoxifen levels, it is unclear what the clinical importance of such reductions may be.

<sup>§</sup> Medications classified as "alternative drugs, expected to have little in vivo inhibition" are not expected to have any effect on endoxifen levels.

<sup>||</sup> Quinidine is mentioned both as a cardiac and an antimalaria medication.

<sup>¶</sup> Not a comprehensive review of all antihistamines.