

**QUALIFICATION MATRIX FOR PREDICTION OF  
DRUG-DRUG INTERACTIONS (DDIs)  
INVOLVING COMPETITIVE AND MECHANISM  
BASED INHIBITION (MBI) OF  
CYP1A2, CYP2C8, CYP2C9, CYP2C19, CYP2D6  
AND CYP3A4  
– SIMCYP SIMULATOR VERSION 19 R1**

December 2024

Certara UK Ltd.

## 1. Contents

1. Contents .....	2
2. Summary.....	3
3. Number of substrates, inhibitors, unique pairs, and DDIs evaluated for the investigated CYPs .....	3
4. List of unique substrate/inhibitor pairs and key characteristics of the compounds .	4
4.1. CYP1A2 list of unique substrate and inhibitor pairs .....	4
4.2. CYP1A2 key characteristics of the substrates and inhibitors .....	4
4.3. CYP2C8 list of unique substrate and inhibitor pairs .....	5
4.4. CYP2C8 key characteristics of the substrates and inhibitors.....	5
4.5. CYP2C9 list of unique substrate and inhibitor pairs .....	6
4.6. CYP2C9 key characteristics of the substrates and inhibitors.....	6
4.7. CYP2C19 list of unique substrate and inhibitor pairs .....	7
4.8. CYP2C19 key characteristics of the substrates and inhibitors .....	7
4.9. CYP2D6 list of unique substrate and inhibitor pairs .....	8
4.10. CYP2D6 key characteristics of the substrates and inhibitors .....	8
4.11. CYP3A4 list of unique substrate and inhibitor pairs.....	9
4.12. CYP3A4 key characteristics of the substrates and inhibitors.....	10
5. The CYP-inhibition qualification matrix .....	11

## 2. Summary

Herein we describe the drug-drug interaction (DDI) matrix that was developed for qualification of the Simcyp Simulator® (V19 R1) with respect to competitive and mechanism-based inhibition (MBI) of CYP1A2, CYP2C8, CYP2C9, CYP2C19, CYP2D6 and CYP3A4/5 to support the following Contexts of Use (COU).

COU1: Simcyp Simulator (V19 R1) can be used to predict the effects of weak and moderate CYP inhibitors on the exposure of a drug when a clinical study with a strong CYP inhibitor has been conducted (and used to verify the fmCYP).

COU2: The Simcyp Simulator (V19 R1) can be used to predict the CYP-mediated inhibitory effect of a drug on the exposure of other CYP substrates when a clinical study with a sensitive CYP substrate has been conducted (and used to verify the competitive inhibition effect *in vivo*).

COU3: The Simcyp Simulator (V19 R1) can be used to predict the CYP-mediated MBI effect of a drug on the exposure of other CYP substrates when a clinical study with a sensitive CYP substrate has been conducted (and used to verify the MBI effect *in vivo*).

The DDI matrix consists of a range of weak, moderate, and strong inhibitors and substrates with varying fraction metabolised by specific CYP enzymes (fmCYP) that were susceptible to different degrees of inhibition. We describe the framework of the DDI matrix, the key characteristics of the drugs, the clinical DDI studies and the predicted *versus* observed interactions.

## 3. Number of substrates, inhibitors, unique pairs, and DDIs evaluated for the investigated CYPs

	No of substrates	No of inhibitors	No of unique pairs	Total No of DDIs
CYP1A2	5	4	11	42
CYP2C8	5	4	10	17
CYP2C9	5	4	10	22
CYP2C19	5	7	12	28
CYP2D6	8	9	27	44
CYP3A4	19	12	54	93

#### 4. List of unique substrate/inhibitor pairs and key characteristics of the compounds

For each enzyme, the number of substrate/inhibitor pairs are recorded in addition to key characteristics of the substrates (CYP contribution – fmCYP (%); bioavailability - F) and inhibitors (dominant inhibitory mechanism). Substrates and inhibitors are assigned as being sensitive/moderately sensitive or having strong/moderate inhibitory potency, respectively, according to categories recommended by the US FDA, CDIS (formerly known as the University of Washington database) and the ICH-M12 guidance.

##### 4.1. CYP1A2 list of unique substrate and inhibitor pairs

<b><i>CYP1A2</i></b>			
<b>Pairs</b>	<b>Substrate</b>	<b>Inhibitor</b>	<b>Studies (n)</b>
1	Caffeine	Cimetidine	2
2	Caffeine	Ciprofloxacin	7
3	Caffeine	Fluvoxamine	3
4	Duloxetine	Fluvoxamine	2
5	Olanzapine	Fluvoxamine	1
6	Theophylline (IV)	Cimetidine	5
7	Theophylline (IV)	Ciprofloxacin	2
8	Theophylline	Cimetidine	8
9	Theophylline	Ciprofloxacin	4
10	Theophylline	Fluvoxamine	4
11	Theophylline	Propranolol	1
12	Theophylline (IV)	Propranolol	1
13	Tizanidine	Ciprofloxacin	1
14	Tizanidine	Fluvoxamine	1
<b>Total DDIs in final matrix</b>			<b>42</b>

##### 4.2. CYP1A2 key characteristics of the substrates and inhibitors

<b>Substrate</b>	<b>FDA</b>	<b>CDIS</b>	<b>ICH-M12</b>	<b>fmCYP1A2 (%)</b>	<b>F</b>
Caffeine	index	sensitive	sensitive	97.9	0.81
Duloxetine		sensitive	sensitive	56.2	0.32
Theophylline		moderate sensitive	moderate sensitive	75.8	0.83
Tizanidine	index	sensitive	sensitive	96.6	0.16
Olanzapine				36.6	0.76
<b>Inhibitor</b>	<b>FDA</b>	<b>CDIS</b>	<b>ICH-M12</b>	<b>INHIBITION</b>	
Ciprofloxacin		strong	moderate	competitive	
Fluvoxamine	strong index	strong	strong	competitive	
Propranolol		moderate	moderate	competitive	
Cimetidine		weak	weak	competitive	

4.3. CYP2C8 list of unique substrate and inhibitor pairs

<u>CYP2C8</u>			
Pairs	Substrate	Inhibitor	Studies (n)
1	Repaglinide	Trimethoprim	1
2	Rosiglitazone	Trimethoprim	2
3	Rosiglitazone	Gemfibrozil	1
4	Pioglitazone	Trimethoprim	3
5	Pioglitazone	Gemfibrozil	4
6	Montelukast	Gemfibrozil	2
7	Pioglitazone	Clopidogrel	1
8	Montelukast	Clopidogrel	1
9	Repaglinide	Tucatinib	1
10	Tucatinib	Gemfibrozil	1
<b>Total DDIs in final Matrix</b>			<b>17</b>

4.4. CYP2C8 key characteristics of the substrates and inhibitors

Substrate	FDA	CDIS	ICH-M12	fmCYP2C8 (%)	F
Repaglinide	sensitive	sensitive	sensitive	66.1	0.76
Rosiglitazone	moderate sensitive	moderate sensitive	moderate sensitive	56.1	0.93
Pioglitazone	moderate sensitive	moderate sensitive	moderate sensitive	64.2	0.74
Montelukast	moderate sensitive	moderate sensitive	moderate sensitive	77.7	0.47
Tucatinib		moderate sensitive	moderate sensitive	71.7	0.26
Inhibitor	FDA	CDIS	ICH-M12	INHIBITION	
Gemfibrozil	strong	strong	strong	competitive	
Gemfibrozil glucuronide				MBI	
Clopidogrel	moderate	moderate	moderate	MBI	
Clopidogrel acyl glucuronide				MBI	
Trimethoprim	weak	weak		competitive	
Tucatinib		weak		competitive	

4.5. CYP2C9 list of unique substrate and inhibitor pairs

<b>CYP2C9</b>			
<b>Pairs</b>	<b>Substrate</b>	<b>Inhibitor</b>	<b>Studies (n)</b>
1	S-Warfarin	Fluconazole	2
2	Tolbutamide	Fluconazole	2
3	Phenytoin	Fluconazole	1
4	Celecoxib	Fluconazole	1
5	Tolbutamide	Fluvoxamine	2
6	Tolbutamide	Sulphaphenazole	1
7	Phenytoin (SD)	Sulphaphenazole	1
8	Flurbiprofen	Fluconazole	9
9	S-Warfarin	Amiodarone	2
10	Phenytoin	Amiodarone	1
<b>Total DDIs in final matrix</b>			<b>22</b>

4.6. CYP2C9 key characteristics of the substrates and inhibitors

<b>Substrate</b>	<b>FDA</b>	<b>CDIS</b>	<b>ICH-M12</b>	<b>fmCYP2C9 (%)</b>	<b>F</b>
Celecoxib	sensitive	sensitive	moderate sensitive	83.5	0.51
Tolbutamide	moderate sensitive	sensitive	moderate sensitive	96.8	0.84
S-Warfarin	moderate sensitive	moderate sensitive	moderate sensitive	98.4	0.86
Flurbiprofen		moderate sensitive	moderate sensitive	81.9	0.92
Phenytoin		moderate sensitive		73.1	0.79
<b>Inhibitor</b>	<b>FDA</b>	<b>CDIS</b>	<b>ICH-M12</b>	<b>INHIBITION</b>	
Sulphaphenazole	N/C	strong	moderate	competitive	
Amiodarone	moderate	moderate	moderate	MBI	
Fluconazole	moderate	moderate	moderate	competitive	
Fluvoxamine	weak	weak	weak	competitive	

4.7. CYP2C19 list of unique substrate and inhibitor pairs

<b>CYP2C19</b>			
<b>Pairs</b>	<b>Substrate</b>	<b>Inhibitor</b>	<b>Studies (n)</b>
1	Imipramine	Fluoxetine	2
2	Lansoprazole	Fluoxetine	5
3	S-Mephenytoin	Fluvoxamine	3
4	Omeprazole	Cimetidine	1
5	Omeprazole	Fluconazole	2
6	Omeprazole	Fluvoxamine	6
7	Omeprazole	Ticlopidine	3
8	Omeprazole	Voriconazole	1
9	Omeprazole	Fluoxetine	2
10	Voriconazole	Omeprazole	1
11	Voriconazole	Cimetidine	1
12	Voriconazole	Fluconazole	1
<b>Total DDIs in final matrix</b>			<b>28</b>

4.8. CYP2C19 key characteristics of the substrates and inhibitors

<b>Substrate</b>	<b>FDA</b>	<b>CDIS</b>	<b>ICH-M12</b>	<b>fmCYP2C19 (%)</b>	<b>F</b>
Lansoprazole	index	sensitive	moderate sensitive	71	0.76
S-Mephenytoin	sensitive	sensitive	sensitive	85.8	0.34
Omeprazole	sensitive	sensitive	sensitive	77.9	0.5
Voriconazole		moderate sensitive	moderate sensitive	69	0.52
Imipramine				38.3	0.38
<b>Inhibitor</b>	<b>FDA</b>	<b>CDIS</b>	<b>ICH-M12</b>	<b>INHIBITION</b>	
Fluvoxamine	index	strong	strong	competitive	
Fluconazole	strong	strong	strong	competitive	
Fluoxetine	strong	strong	strong	MBI	
Nor-fluoxetine				MBI	
Ticlopidine	strong	strong	strong	MBI	
Voriconazole	moderate	moderate		competitive	
Cimetidine	weak	weak	weak	competitive	
Omeprazole	weak	weak		MBI	

4.9. CYP2D6 list of unique substrate and inhibitor pairs

<b>CYP2D6</b>			
<b>Pairs</b>	<b>Substrate</b>	<b>Inhibitor</b>	<b>Studies (n)</b>
1	Atomoxetine	Fluvoxamine	1
2	Atomoxetine	Paroxetine	2
3	Desipramine	Bupropion	1
4	Desipramine	Cinacalcet	1
5	Desipramine	Fluoxetine	3
6	Desipramine	Mirabegron	1
7	Desipramine	Paroxetine	4
8	Desipramine	Cimetidine	1
9	Dextromethorphan	Fluoxetine	1
10	Dextromethorphan	Fluvoxamine	1
11	Dextromethorphan	Quinidine	2
12	Dextromethorphan	Cinacalcet	1
13	Metoprolol	Duloxetine	1
14	Metoprolol	Paroxetine	2
15	Metoprolol	Quinidine	2
16	Metoprolol	Cimetidine	3
17	Nebivolol	Bupropion	1
18	Nebivolol	Fluoxetine	1
19	Nebivolol	Fluvoxamine	1
20	Nebivolol	Paroxetine	1
21	Nebivolol	Cimetidine	1
22	Nebivolol	Duloxetine	1
23	Paroxetine	Cimetidine	2
24	Propranolol	Cimetidine	3
25	Propranolol	Quinidine	3
26	Tolterodine	Fluoxetine	2
27	Tolterodine	Duloxetine	1
<b>Total DDIs in final matrix</b>			<b>44</b>

4.10. CYP2D6 key characteristics of the substrates and inhibitors

<b>Substrate</b>	<b>FDA</b>	<b>CDIS</b>	<b>ICH-M12</b>	<b>fmCYP2D6 (%)</b>	<b>F</b>
Desipramine	index	sensitive	sensitive	81.8	0.44
Dextromethorphan	index	sensitive	sensitive	87.7	0.21
Nebivolol	index	sensitive	sensitive	85.7	0.17
Atomoxetine	sensitive	sensitive	sensitive	78.6	0.61
Tolterodine	sensitive	sensitive	sensitive	82.7	0.29
Propranolol	moderate sensitive	moderate sensitive	moderate sensitive	55.3	0.21
Metoprolol	moderate sensitive	sensitive	moderate sensitive	73.9	0.45
Paroxetine		sensitive		96.7	0.13
<b>Inhibitor</b>	<b>FDA</b>	<b>CDIS</b>	<b>ICH-M12</b>	<b>INHIBITION</b>	
Fluoxetine	index strong	strong	strong	competitive	
Nor-fluoxetine				competitive	
Paroxetine	index strong	strong	strong	MBI	
Bupropion	strong	strong	strong	competitive	
Hydroxy-bupropion				competitive	
Quinidine	strong	strong	strong	competitive	
Cinacalcet	moderate	moderate	moderate	competitive	
Duloxetine	moderate	moderate	moderate	competitive	
Mirabegron	moderate	moderate	moderate	MBI	
Cimetidine	weak	weak	weak	competitive	
Fluvoxamine	weak	weak	weak	competitive	

#### 4.11. CYP3A4 list of unique substrate and inhibitor pairs

<b>CYP3A4</b>			
<b>Pairs</b>	<b>Substrate</b>	<b>Inhibitor</b>	<b>Studies (n)</b>
1	Alfentanil	Fluconazole	6
2	Alfentanil	Ketoconazole	4
3	Alprazolam	Ketoconazole	3
4	Alprazolam	Erythromycin	1
5	Alprazolam	Fluoxetine	1
6	Alprazolam	Cimetidine	2
7	Aprepitant	Ketoconazole	1
8	Atazanavir	Ketoconazole	1
9	Atazanavir	Clarithromycin	1
10	Clarithromycin	Atazanavir	1
11	Dexamethasone	Itraconazole	1
12	Ibrutinib	Ketoconazole	1
13	Ibrutinib	Itraconazole	1
14	Midazolam	Fluconazole	1
15	Midazolam	Itraconazole	3
16	Midazolam	Clarithromycin	1
17	Midazolam	Diltiazem	1
18	Midazolam	Verapamil	1
19	Midazolam	Ketoconazole	6
20	Midazolam	Cimetidine	4
21	Midazolam	Erythromycin	1
22	Midazolam	Fluvoxamine	2
23	Nifedipine	Cimetidine	5
24	Nifedipine	Diltiazem	5
25	Quinidine	Verapamil	2
26	Quinidine	Diltiazem	1
27	Quinidine	Cimetidine	2
28	Quinidine	Itraconazole	2
29	Quinidine	Erythromycin	1
30	Quinidine	Fluvoxamine	1
31	Repaglinide	Itraconazole	1
32	Repaglinide	Clarithromycin	1
33	Rifabutin	Fluconazole	2
34	Rifabutin	Clarithromycin	1
35	Sildenafil	Clarithromycin	1
36	Sildenafil	Erythromycin	1
37	Sildenafil	Cimetidine	1
38	Simvastatin	Diltiazem	1
39	Simvastatin	Amiodarone	1
40	Simvastatin	Erythromycin	1
41	Simvastatin	Verapamil	1
42	Simvastatin	Ketoconazole	1
43	Simvastatin	Clarithromycin	1
44	Triazolam	Diltiazem	1
45	Triazolam	Fluconazole	4
46	Triazolam	Ketoconazole	1
47	Triazolam	Clarithromycin	1
48	Triazolam	Cimetidine	3
49	Triazolam	Erythromycin	1
50	Mirabegron	Ketoconazole	1
51	Carbamazepine	Cimetidine	1
52	Verapamil	Cimetidine	1
53	Zolpidem	Cimetidine	1
54	Alprazolam	Fluvoxamine	1
	<b>Total DDIs in final Matrix</b>		<b>93</b>

#### 4.12. CYP3A4 key characteristics of the substrates and inhibitors

Substrate	FDA	CDIS	ICH-M12	fmCYP3A4 (%)	F
Midazolam	index	sensitive	sensitive	87.6	0.29
Triazolam	index	sensitive	sensitive	90.0	0.51
Alfentanil	sensitive	sensitive	sensitive	91.8	0.34
Ibrutinib	sensitive	sensitive	sensitive	95.0	0.04
Sildenafil	sensitive	sensitive	sensitive	86.0	0.38
Simvastatin	sensitive	sensitive	sensitive	88.7	0.04
Alprazolam	moderate sensitive	moderate sensitive	moderate sensitive	71.0	0.83
Aprepitant	moderate sensitive	moderate sensitive	moderate sensitive	85.2	0.48
Nifedipine		moderate sensitive	moderate sensitive	96.4	0.42
Dexamethasone		moderate sensitive	moderate sensitive	86.1	0.76
Carbamazepine		CYP3A clinically significant NTI substrate		78.9	0.75
Atazanavir		sensitive		74.6	0.36
Clarithromycin		moderate sensitive		73.6	0.51
Quinidine		moderate sensitive		71.7	0.66
Rifabutin		moderate sensitive		66.0	0.11
Verapamil				63.9	0.16
Zolpidem				48.2	0.79
Mirabegron				45.0	0.27
Repaglinide				33.7	0.76
Inhibitor	FDA	CDIS	ICH-M12	INHIBITION	
Clarithromycin	index	strong	strong	MBI	
Itraconazole	index	strong	strong	competitive	
Hydroxy-itraconazole				competitive	
Ketoconazole	strong	strong	strong	competitive	
Diltiazem	moderate	moderate	moderate	MBI	
Desmethyl-diltiazem				MBI	
Erythromycin	moderate	moderate	moderate	MBI	
Fluconazole	moderate	moderate	moderate	competitive	
Verapamil	moderate	moderate	moderate	MBI	
Nor-verapamil				MBI	
Fluvoxamine	moderate	weak	weak	competitive	
Amiodarone	weak	weak	weak	MBI	
Cimetidine	weak	weak		competitive	
Atazanavir		moderate		MBI	
Fluoxetine				MBI	
Nor-fluoxetine				MBI	

## 5. The CYP-inhibition qualification matrix

The composition of the qualification matrix including CYP enzyme, substrate/inhibitor pairs, clinical study design, subject characteristics appears below.

	Enzyme	Substrate	Inhibitor	Substrate dosing	Inhibitor dosing	No. of subjects	Age/ gender	Predicted DDI ratio		Observed DDI ratio		Publication	Link
1	CYP1A2	Caffeine (po)	Ciprofloxacin (po)	3 mg/kg (Day 4 @9:00 AM)	100 mg BID for 4 days (7 doses)	12	20-40 years; 0 F	1.12	1.26	1.07	1.17	Harder et al., 1988	<a href="https://pubmed.ncbi.nlm.nih.gov/2853056/">https://pubmed.ncbi.nlm.nih.gov/2853056/</a>
2	CYP1A2	Caffeine (po)	Ciprofloxacin (po)	3 mg/kg (Day 4 @9:00 AM)	250 mg BID for 4 days (7 doses)	12	20-40 years; 0 F	1.18	1.49	1.09	1.57	Harder et al., 1988	<a href="https://pubmed.ncbi.nlm.nih.gov/2853056/">https://pubmed.ncbi.nlm.nih.gov/2853056/</a>
3	CYP1A2	Caffeine (po)	Ciprofloxacin (po)	3 mg/kg (Day 4 @9:00 AM)	500 mg BID for 4 days (7 doses)	12	20-40 years; 0 F	1.23	1.74	1.17	1.58	Harder et al., 1988	<a href="https://pubmed.ncbi.nlm.nih.gov/2853056/">https://pubmed.ncbi.nlm.nih.gov/2853056/</a>
4	CYP1A2	Caffeine (po)	Ciprofloxacin (po)	183 mg QD for 5 days	750 mg BID for 7 days	12	23-40 years; 50% F	1.46	2.4	1.14	2.45	Mahr et al., 1992	<a href="https://pubmed.ncbi.nlm.nih.gov/1319876/">https://pubmed.ncbi.nlm.nih.gov/1319876/</a>
5	CYP1A2	Caffeine (po)	Fluvoxamine (po)	100 mg (Day 6)	10 mg BID for 6 days	5	22-45 years; 50% F	1.3	3.25	1.68	2.82	Christensen et al., 2002	<a href="https://pubmed.ncbi.nlm.nih.gov/11907488/">https://pubmed.ncbi.nlm.nih.gov/11907488/</a>
6	CYP1A2	Caffeine (po)	Fluvoxamine (po)	100 mg (Day 6)	25 mg BID for 6 days	5	22-45 years; 50% F	1.33	3.9	2.83	5.23	Christensen et al., 2002	<a href="https://pubmed.ncbi.nlm.nih.gov/11907488/">https://pubmed.ncbi.nlm.nih.gov/11907488/</a>
7	CYP1A2	Theophylline (po)	Fluvoxamine (po)	250 mg (Day 8 @8 AM)	25 mg QD for 9 days	9	23-40 years; 44% F	1.07	2.42	1.01	1.44	Yao et al., 2001	<a href="https://pubmed.ncbi.nlm.nih.gov/11719727/">https://pubmed.ncbi.nlm.nih.gov/11719727/</a>
8	CYP1A2	Theophylline (po)	Fluvoxamine (po)	250 mg (Day 8 @8 AM)	50 mg QD on day 1, 75 mg QD days 2-9 (dosed at 4 PM)	9	23-40 years; 44% F	1.08	2.87	1.2	2.03	Yao et al., 2001	<a href="https://pubmed.ncbi.nlm.nih.gov/11719727/">https://pubmed.ncbi.nlm.nih.gov/11719727/</a>
9	CYP1A2	Theophylline (po)	Fluvoxamine (po)	4 mg/kg (Day 6)	50 mg QD days 1-2, 50 mg BID days 3-7	10	19-65; 0 F	1.08	4.01	1.11	2.66	Orlando et al., 2006	<a href="https://pubmed.ncbi.nlm.nih.gov/16678550/">https://pubmed.ncbi.nlm.nih.gov/16678550/</a>

10	<b>CYP1A2</b>	Theophylline (po)	Ciprofloxacin (po)	3.4 mg/kg (Day 4 @9.00 AM)	500 mg BID for 5 days (Day 1 @9.00 PM to Day 5 @9.00 PM) (9 doses)	9	18-36; 56% F	-	1.57	-	1.27	Batty et al., 1995	<a href="https://pubmed.ncbi.nlm.nih.gov/7619673/">https://pubmed.ncbi.nlm.nih.gov/7619673/</a>
11	<b>CYP1A2</b>	Theophylline (IV)	Ciprofloxacin (po)	5 mg/kg IV infusion (30 minutes) (Day 7 @9 AM)	500 mg BID for 7 days (Day 1 @9 AM to Day 7 @9 AM) (13 doses)	8	20-26 years; 0 F	1.01	1.31	1.1	1.33	Prince et al., 1989	<a href="https://pubmed.ncbi.nlm.nih.gov/2760258/">https://pubmed.ncbi.nlm.nih.gov/2760258/</a>
12	<b>CYP1A2</b>	Theophylline (po)	Ciprofloxacin (po)	125 mg TID for 7 days (Day 1 @8 AM to Day 7 @8 AM)	500 mg BID for 7 days (Day 1 @8 AM to Day 7 @8 AM)	9	19-29 years; 0 F	-	1.59	-	1.35	Robson et al., 1990	<a href="https://pubmed.ncbi.nlm.nih.gov/2328197/">https://pubmed.ncbi.nlm.nih.gov/2328197/</a>
13	<b>CYP1A2</b>	Theophylline (IV)	Ciprofloxacin (po)	5 mg/kg SD IV infusion (30 minutes) (Day 5 @7 AM)	500 mg BID for 7 days (Day 1 @7 AM to Day 7 @7 PM) (14 doses)	6	22-35 years; 0 F	-	1.51	-	1.48	Loi et al., 1993	<a href="https://pubmed.ncbi.nlm.nih.gov/9114903/">https://pubmed.ncbi.nlm.nih.gov/9114903/</a>
14	<b>CYP1A2</b>	Caffeine (po)	Ciprofloxacin (po)	100 mg (Day 2 @9 AM)	750 mg BID for 2 days (3 doses)	10	24-29 years; 0 F	1.26	1.93	1.1	1.59	Healy et al., 1989	<a href="https://pubmed.ncbi.nlm.nih.gov/2729942/">https://pubmed.ncbi.nlm.nih.gov/2729942/</a>
15	<b>CYP1A2</b>	Tizanidine (po)	Fluvoxamine (po)	4 mg (Day 4, 1h after Fluvoxamine)	100 mg QD for 4 days	10	21-31 years; 0 F	9.85	32.37	12.09	32.73	Gransfor et al., 2004	<a href="https://pubmed.ncbi.nlm.nih.gov/15060511/">https://pubmed.ncbi.nlm.nih.gov/15060511/</a>
16	<b>CYP1A2</b>	Tizanidine (po)	Ciprofloxacin (po)	4 mg (Day 3, 1h after Ciprofloxacin dose)	500 mg BID for 3 days	10	22-28 years; 0F	3.12	3.36	6.83	9.74	Gransfor et al., 2004	<a href="https://pubmed.ncbi.nlm.nih.gov/15592331/">https://pubmed.ncbi.nlm.nih.gov/15592331/</a>
17	<b>CYP1A2</b>	Caffeine (po)	Cimetidine (po)	300 mg on Day 6	200 mg TID and 400 mg at night for 6 days	5	20-21 years; 40% F	-	1.58	-	1.38	Broughton et al., 1981	<a href="https://doi.org/10.1111/j.1365-2125.1981.tb01194">https://doi.org/10.1111/j.1365-2125.1981.tb01194</a>
18	<b>CYP1A2</b>	Caffeine (po)	Cimetidine (po)	2mg/kg on Day 4	300 mg QID for 4 days	6	21-50 years; 0 F	-	1.64	-	1.73	May et al., 1982	<a href="https://doi.org/10.1038/clpt.1982.91">DOI: 10.1038/clpt.1982.91</a>
19	<b>CYP1A2</b>	Caffeine (po)	Ciprofloxacin (po)	230 mg on Day 4	250 mg BID for 4 days	12	24-39 years	1.19	1.49	1.09	1.57	Staib et al., 1987	<a href="https://pubmed.ncbi.nlm.nih.gov/3481318/">https://pubmed.ncbi.nlm.nih.gov/3481318/</a>
20	<b>CYP1A2</b>	Caffeine (po)	Ciprofloxacin (po)	100 mg TID for 3 days	500 mg BID for 3 days	24	20-40 years; 50% F	1.55	1.91	1.59	2.27	Nicolau et al., 1985	<a href="https://pubmed.ncbi.nlm.nih.gov/8549360/">https://pubmed.ncbi.nlm.nih.gov/8549360/</a>
21	<b>CYP1A2</b>	Caffeine (po)	Fluvoxamine (po)	200 mg on Day 8	50 mg for 4 days and 100 mg for 8 days	8	21-33 years; 0 F	-	12.74	-	8.36	Jeppesen et al., 1996	<a href="https://pubmed.ncbi.nlm.nih.gov/8807660/">https://pubmed.ncbi.nlm.nih.gov/8807660/</a>

22	<b>CYP1A2</b>	Theophylline (IV)	Cimetidine (po)	5 mg/kg (IV) on Day 7	300 mg QID for 6 days	10	20-40 years; 50% F	-	1.44	-	1.41	Lin et al., 1987	<a href="https://pubmed.ncbi.nlm.nih.gov/2893637/">https://pubmed.ncbi.nlm.nih.gov/2893637/</a>
23	<b>CYP1A2</b>	Theophylline (IV)	Cimetidine (po)	3 mg/kg (IV) on Day 7	200 mg TID and 400 mg at night for 6 days	7	26-52 years; 29% F	-	1.42	-	1.41	Roberts et al., 1981	<a href="https://pubmed.ncbi.nlm.nih.gov/7239117/">https://pubmed.ncbi.nlm.nih.gov/7239117/</a>
24	<b>CYP1A2</b>	Theophylline (IV)	Cimetidine (po)	6 mg/kg (IV) on Day 3	300 mg QID for 2.75 days	5	27-33 years; 0 F	-	1.29	-	1.67	Jackson et al., 1981	<a href="https://pubmed.ncbi.nlm.nih.gov/7023306/">https://pubmed.ncbi.nlm.nih.gov/7023306/</a>
25	<b>CYP1A2</b>	Theophylline (IV)	Cimetidine (po)	6 mg/kg (IV) on Day 4	300 mg QID for 5 days	12	20-29 years; 0 F	-	1.47	-	1.56	Powell et al., 1984	<a href="https://pubmed.ncbi.nlm.nih.gov/6322709/">https://pubmed.ncbi.nlm.nih.gov/6322709/</a>
26	<b>CYP1A2</b>	Theophylline (IV)	Cimetidine (po)	3 mg/Kg, 30 min IV infusion	200 mg TID and 400 mg at night for 7 days	7	20-40 years; 0 F	-	1.37	-	1.54	Breen et al., 1982	<a href="https://pubmed.ncbi.nlm.nih.gov/6120774/">https://pubmed.ncbi.nlm.nih.gov/6120774/</a>
27	<b>CYP1A2</b>	Theophylline (IV)	Cimetidine (po)	5 mg/kg on Day 8	300 mg QID for 10 days	14	19-56 years; 50% F	-	1.44	-	1.36	Jennings et al., 1993	<a href="https://pubmed.ncbi.nlm.nih.gov/8340707/">https://pubmed.ncbi.nlm.nih.gov/8340707/</a>
28	<b>CYP1A2</b>	Theophylline (IV)	Cimetidine (po)	5 mg/kg SD IV infusion (30 minutes) (Day 5 @7 AM)	400 mg BID for 7 days (Day 1 @7 AM to Day 7 @7 PM) (14 doses)	6	22-35 years; 0 F	-	1.29	-	1.34	Loi_1993 et al., 1993	<a href="https://pubmed.ncbi.nlm.nih.gov/9114903/">https://pubmed.ncbi.nlm.nih.gov/9114903/</a>
29	<b>CYP1A2</b>	Theophylline (po)	Cimetidine (po)	250 mg on Day 7 @8 AM	400 mg BID for 8 days	6	25-40 years; 0 F	-	1.30	-	1.64	Naline et al., 1988	<a href="https://pubmed.ncbi.nlm.nih.gov/3265407/">https://pubmed.ncbi.nlm.nih.gov/3265407/</a>
30	<b>CYP1A2</b>	Duloxetine (po)	Fluvoxamine (po)	60 mg dose on Day 14 and 20 (7 and 13)	50 mg on Day 1 followed by 100 mg for 16 days.	14	18-65 years; 0 F	2.42	5.54	2.41	5.6	Lobo et al., 2008	<a href="https://pubmed.ncbi.nlm.nih.gov/18307373/">https://pubmed.ncbi.nlm.nih.gov/18307373/</a>
31	<b>CYP1A2</b>	Duloxetine (IV)	Fluvoxamine (po)	10 mg IV dose on Day 14 and 20 (7 and 13)	50 mg on Day 1 followed by 100 mg for 16 days.	14	18-65 years; 0 F	1.01	2.39	0.84	2.7	Lobo et al., 2008	<a href="https://pubmed.ncbi.nlm.nih.gov/18307373/">https://pubmed.ncbi.nlm.nih.gov/18307373/</a>
32	<b>CYP1A2</b>	Theophylline (po)	Propranolol (po)	125 mg TID for 10 days	240 mg TID from Day 6 to 10	7	19-30 years; 0 F	-	2.12	-	2.07	Miners et al., 1985	<a href="https://pubmed.ncbi.nlm.nih.gov/4041342/">https://pubmed.ncbi.nlm.nih.gov/4041342/</a>
33	<b>CYP1A2</b>	Theophylline (IV)	Propranolol (po)	6 mg/kg infusion given on day 2	40 mg QID for 3 days	6	24-33 years; 0 F	-	1.43	-	1.33	Conrad et al., 1980	<a href="https://pubmed.ncbi.nlm.nih.gov/7408406/">https://pubmed.ncbi.nlm.nih.gov/7408406/</a>
34	<b>CYP1A2</b>	Theophylline (po)	Cimetidine (po)	4 mg/kg oral on Day 8	300 mg QID for 8 days	6	23-31 years; 0 F	-	1.37	-	1.46	Reitberg et al., 1981	<a href="https://pubmed.ncbi.nlm.nih.gov/7294546/">https://pubmed.ncbi.nlm.nih.gov/7294546/</a>
35	<b>CYP1A2</b>	Theophylline (po)	Cimetidine (po)	200 mg oral every 6 hours for 10 days	300 mg QID for 7 days starting on Day 3	7	22-33 years; 0 F	-	1.53	-	1.39	Lalonde et al., 1983	<a href="https://pubmed.ncbi.nlm.nih.gov/6822105/">https://pubmed.ncbi.nlm.nih.gov/6822105/</a>

36	<b>CYP1A2</b>	Theophylline (po)	Cimetidine (po)	170 mg oral every 8 hours for 14 days	400 mg TID for 7 days starting on Day 8	6	19-31 years; 0 F	-	1.46	-	1.47	Cusack et al., 1985	<a href="https://pubmed.ncbi.nlm.nih.gov/3971657/">https://pubmed.ncbi.nlm.nih.gov/3971657/</a>
37	<b>CYP1A2</b>	Theophylline (po)	Cimetidine (po)	170 mg oral every 8 hours for 14 days	400 mg TID for 7 days starting on Day 8	10	19-31 years; 0 F	-	1.46	-	1.41	Vestal et al., 1987	<a href="https://pubmed.ncbi.nlm.nih.gov/3572808/">https://pubmed.ncbi.nlm.nih.gov/3572808/</a>
38	<b>CYP1A2</b>	Theophylline (po)	Cimetidine (po)	200 mg oral on day 3, 1 hour after cimetidine	400 mg TID for 3 days	9	24-42 years; 0 F	-	1.22	-	1.36	Ohashi et al., 1993	<a href="https://pubmed.ncbi.nlm.nih.gov/8126258/">https://pubmed.ncbi.nlm.nih.gov/8126258/</a>
39	<b>CYP1A2</b>	Olanzapine (po)	Fluvoxamine (po)	10 mg on day 4	100 mg QD for 9 days	21	20-50 years; 0 F Chinese	1.12	1.54	1.49	1.76	Wang et al., 2004	<a href="https://pubmed.ncbi.nlm.nih.gov/15199083/">https://pubmed.ncbi.nlm.nih.gov/15199083/</a>
40	<b>CYP1A2</b>	Theophylline (po)	Ciprofloxacin (po)	200 mg BID (7 am and 7 pm) for 10 days	750 mg BID starting on Day 4 until Day 8 (7 am last dose)	8	21-26 years; 0 F	-	1.79	-	1.49	Schwartz et al., 1998	<a href="https://pubmed.ncbi.nlm.nih.gov/3348614/">https://pubmed.ncbi.nlm.nih.gov/3348614/</a>
41	<b>CYP1A2</b>	Theophylline (po)	Ciprofloxacin (po)	400 mg dose on day 6	500 mg BID for 7 days	8	22-28 years; 0 F	-	1.52	-	1.44	Gillum et al., 1996	<a href="https://pubmed.ncbi.nlm.nih.gov/8807068/">https://pubmed.ncbi.nlm.nih.gov/8807068/</a>
42	<b>CYP1A2</b>	Theophylline (po)	Fluvoxamine (po)	300 mg dose on day 4	50 mg on day 1, 100 mg QD for 6 days	12	22-30 years; 0 F	-	3.72	-	3.33	Rasmussen et al., 1996	<a href="https://pubmed.ncbi.nlm.nih.gov/9029748/">https://pubmed.ncbi.nlm.nih.gov/9029748/</a>
43	<b>CYP2C8</b>	Repaglinide (po)	Trimethoprim (po)	0.25 mg on day 3 at 9 AM	160 mg BID for 3 days at 8 AM and 8 PM	9	19-23 years; 11% F	1.24	1.37	1.40	1.59	Niemi et al., 2004	<a href="https://pubmed.ncbi.nlm.nih.gov/15025742/">https://pubmed.ncbi.nlm.nih.gov/15025742/</a>
44	<b>CYP2C8</b>	Rosiglitazone (po)	Trimethoprim (po)	4 mg on day 3 at 9 AM	160 mg BID for 4 days (at 8 AM and 8 PM on day 1, 2, 4; at 8 AM and 9 PM on day 3)	12	20-24 years; 67% F	1.08	1.40	1.14	1.37	Niemi et al., 2003	<a href="https://pubmed.ncbi.nlm.nih.gov/12687332/">https://pubmed.ncbi.nlm.nih.gov/12687332/</a>
45	<b>CYP2C8</b>	Rosiglitazone (po)	Trimethoprim (po)	8 mg on day 4 at 8 AM	200 mg BID for 5 days (at 7:30 AM and 7:30 PM), (9 doses)	8	21-57 years; 50% F	1.10	1.48	0.88	1.31	Hruska et al., 2005	<a href="https://pubmed.ncbi.nlm.nih.gov/15606443/">https://pubmed.ncbi.nlm.nih.gov/15606443/</a>
46	<b>CYP2C8</b>	Rosiglitazone (po)	Gemfibrozil (po)	4 mg at 9 AM on day 3	600 mg BID at 8 AM and 8 PM for 7 doses	10	21-26 years; 10% F	1.17	2.38	1.22	2.29	Niemi et al., 2003	<a href="https://pubmed.ncbi.nlm.nih.gov/12898007/">https://pubmed.ncbi.nlm.nih.gov/12898007/</a>

47	<b>CYP2C8</b>	Pioglitazone (po)	Trimethoprim (po)	15 mg on day 3 (1h after the 5th dose of inhibitor)	160 mg BID for 6 days	8	19-25 years; 50% F, *1*1	1.08	1.44	1.10	1.37	Tornio et al., 2008	<a href="https://pubmed.ncbi.nlm.nih.gov/17913794/">https://pubmed.ncbi.nlm.nih.gov/17913794/</a>
48	<b>CYP2C8</b>	Pioglitazone (po)	Trimethoprim (po)	15 mg on day 3 (1h after the 5th dose of inhibitor)	160 mg BID for 6 days	5	19-25 years; 40% F, *1*3	1.12	1.51	1.25	1.55	Tornio et al., 2008	<a href="https://pubmed.ncbi.nlm.nih.gov/17913794/">https://pubmed.ncbi.nlm.nih.gov/17913794/</a>
49	<b>CYP2C8</b>	Pioglitazone (po)	Trimethoprim (po)	15 mg on day 3 (1h after the 5th dose of inhibitor)	160 mg BID for 6 days	3	19-25 years; 67% F, *3*3	1.12	1.52	1.16	1.40	Tornio et al., 2008	<a href="https://pubmed.ncbi.nlm.nih.gov/17913794/">https://pubmed.ncbi.nlm.nih.gov/17913794/</a>
50	<b>CYP2C8</b>	Pioglitazone (po)	Gemfibrozil (po)	15 mg on day 3 at 9 AM	600 mg BID (8AM and 8PM) for 4 days	12	20-27 years; 25% F	1.17	2.69	1.06	3.22	Jaakola et al., 2005	<a href="https://pubmed.ncbi.nlm.nih.gov/15900286/">https://pubmed.ncbi.nlm.nih.gov/15900286/</a>
51	<b>CYP2C8</b>	Pioglitazone (po)	Gemfibrozil (po)	30 mg on day 3 at 8 AM	600 mg BID (7AM and 7PM) for 7 days	10	22-23 years; 0 F	1.06	1.62	1.11	3.38	Deng et al., 2005	<a href="https://pubmed.ncbi.nlm.nih.gov/16283275/">https://pubmed.ncbi.nlm.nih.gov/16283275/</a>
52	<b>CYP2C8</b>	Pioglitazone (po)	Gemfibrozil (po)	15 mg on day 3 at 9 AM	600 mg BID at 8AM and 8PM for 4 days	15	21-50; 73% F, *1*1	1.17	2.69	1.09	3.12	Aquilante et al., 2013	<a href="https://pubmed.ncbi.nlm.nih.gov/22625877/">https://pubmed.ncbi.nlm.nih.gov/22625877/</a>
53	<b>CYP2C8</b>	Pioglitazone (po)	Gemfibrozil (po)	15 mg on day 3 at 9 AM	601 mg BID at 8AM and 8PM for 4 days	15	21-60; 87% F, *3*3	1.23	3.25	1.15	4.66	Aquilante et al., 2013	<a href="https://pubmed.ncbi.nlm.nih.gov/22625877/">https://pubmed.ncbi.nlm.nih.gov/22625877/</a>
54	<b>CYP2C8</b>	Montelukast (po)	Gemfibrozil (po)	10 mg on day 3 (1 hr after Gemfibrozil)	600 mg BID for 5 days	11	21-29 years; 27% F	1.96	3.74	1.46	4.28	Karonen et al., 2012	<a href="https://pubmed.ncbi.nlm.nih.gov/21838784/">https://pubmed.ncbi.nlm.nih.gov/21838784/</a>
55	<b>CYP2C8</b>	Montelukast (po)	Gemfibrozil (po)	10 mg on day 3 (1 hr after Gemfibrozil)	600 mg BID for 3 days	10	20-26 years; 40% F	2.09	3.96	1.53	4.54	Karonen et al., 2010	<a href="https://pubmed.ncbi.nlm.nih.gov/20592724/">https://pubmed.ncbi.nlm.nih.gov/20592724/</a>
56	<b>CYP2C8</b>	Repaglinide (po)	Clopidogrel (po)	0.25 mg on day 3 (1 h after Clopidogrel dosing)	300 mg on day 1, 75 mg on days 2 and 3, 8AM (3 doses)	9	19-30 years; 44% F	1.85	2.70	2.53	5.08	Tornio et al., 2014	<a href="https://pubmed.ncbi.nlm.nih.gov/24971633/">https://pubmed.ncbi.nlm.nih.gov/24971633/</a>
57	<b>CYP2C8</b>	Montelukast (po)	Clopidogrel (po)	10 mg on day 1 (1 hr after Clopidogrel)	300 mg on day 1, 75 mg on day 2, 8AM (2 doses)	12	19-31 years; 58% F	1.74	3.11	0.98	1.98	Itkonen et al., 2018	<a href="https://pubmed.ncbi.nlm.nih.gov/29171020/">https://pubmed.ncbi.nlm.nih.gov/29171020/</a>

58	<b>CYP2C8</b>	Tucatinib (po)	Gemfibrozil (po)	300 mg on day 5 at 8AM	600 mg BID on days 1-6, 8AM	26	18-65 years; 100% F	1.69	3.26	1.62	3.04	Topletz et al., 2022	<a href="https://pubmed.ncbi.nlm.nih.gov/35931943/">https://pubmed.ncbi.nlm.nih.gov/35931943/</a>
59	<b>CYP2C8</b>	Repaglinide (po)	Tucatinib (po)	0.5 mg on day 8 at 8AM	300 mg BID on day 1-10, 8AM and 8PM	26	18-65 years; 100% F	1.34	1.67	1.69	1.69	Topletz et al., 2022	<a href="https://pubmed.ncbi.nlm.nih.gov/35931943/">https://pubmed.ncbi.nlm.nih.gov/35931943/</a>
60	<b>CYP2C9</b>	S-Warfarin (po)	Fluconazole (po)	0.375 mg/kg on day 7 (1hr before Fluconazole)	400 mg QD for 14 days	6	23-29 years; 0 F	-	2.72	-	2.90	Black et al., 1996	<a href="https://pubmed.ncbi.nlm.nih.gov/8801057/">https://pubmed.ncbi.nlm.nih.gov/8801057/</a>
61	<b>CYP2C9</b>	S-Warfarin (po)	Fluconazole (po)	8.75 mg on day 14	400 mg QD for 20 days	10	21-52; 10% F	1.07	2.56	1.15	2.56	Bavisotto et al., 2011	<a href="https://pubmed.ncbi.nlm.nih.gov/20622200/">https://pubmed.ncbi.nlm.nih.gov/20622200/</a>
62	<b>CYP2C9</b>	Tolbutamide (po)	Fluconazole (po)	500 mg 2hrs after Fluconazole	150 mg SD	13	20-50 years; 0 F	1.09	1.31	1.23	1.90	Lazar et al., 1990	<a href="https://pubmed.ncbi.nlm.nih.gov/2330488/">https://pubmed.ncbi.nlm.nih.gov/2330488/</a>
63	<b>CYP2C9</b>	Tolbutamide (po)	Fluconazole (po)	500 mg on day 8 (2hrs after fluconazole)	150 mg on day 1 and 100 mg QD days 2 - 8	13	20-50 years; 0 F	1.13	1.51	1.30	2.09	Lazar et al., 1990	<a href="https://pubmed.ncbi.nlm.nih.gov/2330488/">https://pubmed.ncbi.nlm.nih.gov/2330488/</a>
64	<b>CYP2C9</b>	Phenytoin (po)	Fluconazole (po)	250 mg on day 5 (8AM)	400 mg QD for 6 days (8AM)	9	22-35 years; 0 F	-	1.40	-	1.33	Touchette et al., 1992	<a href="https://pubmed.ncbi.nlm.nih.gov/1633070/">https://pubmed.ncbi.nlm.nih.gov/1633070/</a>
65	<b>CYP2C9</b>	Celecoxib (po)	Fluconazole (po)	200 mg on day 7	200 mg QD for 7 days	17	20-50 years; 50% F	1.33	1.9	1.68	2.34	FDA	NDA #20998 Clinical pharmacology/biopharmaceutics review section Celecoxib. (1998). - PART 2
66	<b>CYP2C9</b>	Tolbutamide (po)	Fluvoxamine (po)	500 mg on day 5 (8.00 am)	75 mg QD for 5 days (dosed at 8.00 pm)	7	21-30 years; 0 F	-	1.37	-	1.23	Madsen et al., 2001	<a href="https://pubmed.ncbi.nlm.nih.gov/11180037/">https://pubmed.ncbi.nlm.nih.gov/11180037/</a>
67	<b>CYP2C9</b>	Tolbutamide (po)	Fluvoxamine (po)	500 mg on day 5 (8.00 am)	150 mg QD for 5 days (dosed at 8.00 pm)	7	21-30 years; 0 F	-	1.66	-	1.71	Madsen et al., 2001	<a href="https://pubmed.ncbi.nlm.nih.gov/11180037/">https://pubmed.ncbi.nlm.nih.gov/11180037/</a>
68	<b>CYP2C9</b>	Tolbutamide (IV)	Sulphaphenazole (po)	500 mg IV 30 sec bolus on day 4 @10am	500 mg BID for 4 days @ 9am and 9pm (7 doses)	7	21-33 years; 57% F	-	3.78	-	3.10	Back et al., 1988	<a href="https://pubmed.ncbi.nlm.nih.gov/3383988/">https://pubmed.ncbi.nlm.nih.gov/3383988/</a>
69	<b>CYP2C9</b>	Phenytoin (IV)	Sulphaphenazole (po)	100 mg IV on day 7	2000 mg QD for 7 days	13	20-50 years; 50% F	-	2.29	-	1.83	Hansen et al., 1979	<a href="https://pubmed.ncbi.nlm.nih.gov/284708/">https://pubmed.ncbi.nlm.nih.gov/284708/</a>

70	<b>CYP2C9</b>	Flurbiprofen (po)	Fluconazole (po)	100 mg (0.5 hrs after last dose Fluconazole)	200 mg 2 doses, 14.5 hours apart	12	19-54 years; 25% F	1.1	1.71	1.16	1.62	Hanley et al., 2013	<a href="https://pubmed.ncbi.nlm.nih.gov/22943633/">https://pubmed.ncbi.nlm.nih.gov/22943633/</a>
71	<b>CYP2C9</b>	S-Warfarin (po)	Amiodarone (po)	0.375 mg/kg on day 3	300 mg QD (3 doses), 284 mg base	5	21-35 years; 0 F	-	1.22	-	1.27	Heimark et al., 1992	<a href="https://pubmed.ncbi.nlm.nih.gov/1563209/">https://pubmed.ncbi.nlm.nih.gov/1563209/</a>
72	<b>CYP2C9</b>	S-Warfarin (po)	Amiodarone (po)	0.75 mg/kg on day 4	200 mg BID for duration of study, 189 mg base	6	21-35 years; 0 F	-	2.04	-	2.11	O'Reilly et al., 1987	<a href="https://pubmed.ncbi.nlm.nih.gov/3621782/">https://pubmed.ncbi.nlm.nih.gov/3621782/</a>
73	<b>CYP2C9</b>	Phenytoin (IV)	Amiodarone (po)	5 mg/kg IV infusion (30 min) (At SS of Amiodarone)	200 mg QD for duration of study (189 mg base)	7	24-36 years; 0 F	-	1.37	-	1.37	Nolan et al., 1989	<a href="https://pubmed.ncbi.nlm.nih.gov/2743707/">https://pubmed.ncbi.nlm.nih.gov/2743707/</a>
74	<b>CYP2C9</b>	Flurbiprofen (po)	Fluconazole (po)	50 mg on day 7 (2h after Fluconazole)	200 mg QD at 8am for 7 days	11	19-36 years; 64% F, *1*1	1.13	2	0.78	2.02	Kumar et al., 2008	<a href="https://pubmed.ncbi.nlm.nih.gov/18378563/">https://pubmed.ncbi.nlm.nih.gov/18378563/</a>
75	<b>CYP2C9</b>	Flurbiprofen (po)	Fluconazole (po)	50 mg on day 7 (2h after Fluconazole)	400 mg QD at 8am for 7 days	11	19-36 years; 64% F, *1*1	1.17	2.84	0.99	3.03	Kumar et al., 2008	<a href="https://pubmed.ncbi.nlm.nih.gov/18378563/">https://pubmed.ncbi.nlm.nih.gov/18378563/</a>
76	<b>CYP2C9</b>	Flurbiprofen (po)	Fluconazole (po)	50 mg on day 7 (2h after Fluconazole)	200 mg QD at 8am for 7 days	8	19-28 years; 63% F, *1*3	1.08	1.82	0.87	1.79	Kumar et al., 2008	<a href="https://pubmed.ncbi.nlm.nih.gov/18378563/">https://pubmed.ncbi.nlm.nih.gov/18378563/</a>
77	<b>CYP2C9</b>	Flurbiprofen (po)	Fluconazole (po)	50 mg on day 7 (2h after Fluconazole)	400 mg QD at 8am for 7 days	8	19-28 years; 63% F, *1*3	1.11	2.46	0.94	2.48	Kumar et al., 2008	<a href="https://pubmed.ncbi.nlm.nih.gov/18378563/">https://pubmed.ncbi.nlm.nih.gov/18378563/</a>
78	<b>CYP2C9</b>	Flurbiprofen (po)	Fluconazole (po)	Flurbiprofen, 50 mg SD day 7 (2h after Fluconazole)	Fluconazole, 200 mg QD at 8am for 7 days	2	25-29 years; 0 F, *3*3	1.02	1.33	0.99	1.41	Kumar et al., 2008	<a href="https://pubmed.ncbi.nlm.nih.gov/18378563/">https://pubmed.ncbi.nlm.nih.gov/18378563/</a>
79	<b>CYP2C9</b>	Flurbiprofen (po)	Fluconazole (po)	Flurbiprofen, 50 mg SD day 7 (2h after Fluconazole)	Fluconazole, 400 mg QD at 8am for 7 days	2	25-29 years; 0 F, *3*3	1.03	1.58	0.74	1.23	Kumar et al., 2008	<a href="https://pubmed.ncbi.nlm.nih.gov/18378563/">https://pubmed.ncbi.nlm.nih.gov/18378563/</a>
80	<b>CYP2C9</b>	Flurbiprofen	Fluconazole	Flurbiprofen, 50 mg SD day 1 (2h after Fluconazole)	Fluconazole, 400 mg QD at 8am for 7 days	12	32-34 years; 58% F	1.11	1.88	1.24	2.16	Zgheib et al., 2007	<a href="https://pubmed.ncbi.nlm.nih.gov/17054666/">https://pubmed.ncbi.nlm.nih.gov/17054666/</a>

81	<b>CYP2C9</b>	Flurbiprofen	Fluconazole	Flurbiprofen, 50 mg SD day 7 (2h after Fluconazole)	Fluconazole, 400 mg QD at 8am for 7 days	12	32-34 years; 58% F	1.17	2.76	1.37	2.80	Zgheib et al., 2007	<a href="https://pubmed.ncbi.nlm.nih.gov/17054666/">https://pubmed.ncbi.nlm.nih.gov/17054666/</a>
82	<b>CYP2C19</b>	S-Mephenytoin (po)	Fluvoxamine (po)	100 mg SD on day 9 (8 AM)	37.5 mg QD for 11 days (dosed at 4 PM)	12	23-49 years; 42% F	2.15	5.41	2.12	4.64	Yao et al., 2003	<a href="https://pubmed.ncbi.nlm.nih.gov/12695344/">https://pubmed.ncbi.nlm.nih.gov/12695344/</a>
83	<b>CYP2C19</b>	S-Mephenytoin (po)	Fluvoxamine (po)	101 mg SD on day 9 (8 AM)	62.5 mg QD for 11 days (dosed at 4 PM)	12	23-49 years; 42% F	2.45	8.21	2.4	6.7	Yao et al., 2003	<a href="https://pubmed.ncbi.nlm.nih.gov/12695344/">https://pubmed.ncbi.nlm.nih.gov/12695344/</a>
84	<b>CYP2C19</b>	S-Mephenytoin (po)	Fluvoxamine (po)	102 mg SD on day 9 (8 AM)	50 mg QD (days 1-2), 87.5 mg QD (days 3-11) (dosed at 4 PM)	12	23-49 years; 42% F	2.64	10.99	2.42	9.89	Yao et al., 2003	<a href="https://pubmed.ncbi.nlm.nih.gov/12695344/">https://pubmed.ncbi.nlm.nih.gov/12695344/</a>
85	<b>CYP2C19</b>	Omeprazole (po)	Fluvoxamine (po)	20 mg SD day7	25 mg BID for 7 days	6	22-45 years; 50% F	-	4.86	-	5.46	Christensen et al., 2002	<a href="https://pubmed.ncbi.nlm.nih.gov/11907488/">https://pubmed.ncbi.nlm.nih.gov/11907488/</a>
86	<b>CYP2C19</b>	Imipramine (po)	Fluoxetine (po)	44.26 mg SD (3hrs after Fluoxetine)	60 mg SD	6	28-51 years; 0 F	1.25	1.52	1.23	1.89	Bergstrom et al., 1992	<a href="https://pubmed.ncbi.nlm.nih.gov/1544284/">https://pubmed.ncbi.nlm.nih.gov/1544284/</a>
87	<b>CYP2C19</b>	Imipramine (po)	Fluoxetine (po)	44.26 mg SD on day 8 (3hrs after Fluoxetine)	60 mg QD for 8 days	6	28-51 years; 0 F	1.8	3.28	1.75	3.33	Bergstrom et al., 1992	<a href="https://pubmed.ncbi.nlm.nih.gov/1544284/">https://pubmed.ncbi.nlm.nih.gov/1544284/</a>
88	<b>CYP2C19</b>	Omeprazole (po)	Ticlopidine (po)	20 mg SD (on day 8) 1h after Ticlopidine	200 mg ticlopidine HCL QD for 8 days at 8 AM	6	20-33 years; 50% F, Japanese, EM	2.22	5.22	2.99	6.22	Leiri et al., 2005	<a href="https://pubmed.ncbi.nlm.nih.gov/16272957/">https://pubmed.ncbi.nlm.nih.gov/16272957/</a>
89	<b>CYP2C19</b>	Omeprazole (po)	Ticlopidine (po)	40 mg SD on day 7	100 mg of ticlopidine HCL TID (19 doses)	6	24-43 years; 0 F, Japanese	2.42	4.23	2.11	2.4	Tateishi et al., 1997	<a href="https://pubmed.ncbi.nlm.nih.gov/10233213/">https://pubmed.ncbi.nlm.nih.gov/10233213/</a>
90	<b>CYP2C19</b>	Omeprazole (po)	Fluvoxamine (po)	20 mg SD day7	25 mg QD for 7 days	5	22-45 years; 50% F, PM	-	5.34	-	5.85	Christensen et al., 2002	<a href="https://pubmed.ncbi.nlm.nih.gov/11907488/">https://pubmed.ncbi.nlm.nih.gov/11907488/</a>
91	<b>CYP2C19</b>	Omeprazole (po)	Fluvoxamine (po)	20 mg SD day7	10mg BID for 7 days	6	22-45 years; 50% F, EM	-	3.15	-	2.63	Christensen et al., 2002	<a href="https://pubmed.ncbi.nlm.nih.gov/11907488/">https://pubmed.ncbi.nlm.nih.gov/11907488/</a>

92	<b>CYP2C19</b>	Omeprazole (po)	Fluvoxamine (po)	20 mg SD day7	10mg QD for 7 days	7	22-45 years; 50% F, PM	-	3.46	-	2.43	Christensen et al., 2002	<a href="https://pubmed.ncbi.nlm.nih.gov/11907488/">https://pubmed.ncbi.nlm.nih.gov/11907488/</a>
93	<b>CYP2C19</b>	Omeprazole (po)	Ticlopidine (po)	20 mg SD (on day 8) 1h after Ticlopidine	200 mg QD at 8 AM	6	20-33 years; 50% F, Japanese, IM	2.01	4.72	3.38	5.01	Leiri et al., 2005	<a href="https://pubmed.ncbi.nlm.nih.gov/16272957/">https://pubmed.ncbi.nlm.nih.gov/16272957/</a>
94	<b>CYP2C19</b>	Lansoprazole (po)	Fluoxetine (po)	60 mg SD on day 6	25 mg BID for 6 days	6	21-29 years; 50% F, Japanese, EM	1.57	4.26	1.54	3.83	Niioka et al., 2006	<a href="https://pubmed.ncbi.nlm.nih.gov/16778714/">https://pubmed.ncbi.nlm.nih.gov/16778714/</a>
95	<b>CYP2C19</b>	Lansoprazole (po)	Fluoxetine (po)	60 mg SD on day 6	25 mg BID for 6 days	6	21-29 years; 50% F, Japanese, IM	1.4	3.44	1.21	2.5	Niioka et al., 2006	<a href="https://pubmed.ncbi.nlm.nih.gov/16778714/">https://pubmed.ncbi.nlm.nih.gov/16778714/</a>
96	<b>CYP2C19</b>	Lansoprazole (po)	Fluoxetine (po)	30 mg SD on day 8	60 mg QD for 8 days	18	24-30 years; 0 F	1.51	3.24	1.68	2.94	Vlase et al., 2011	<a href="https://pubmed.ncbi.nlm.nih.gov/21877765/">https://pubmed.ncbi.nlm.nih.gov/21877765/</a>
97	<b>CYP2C19</b>	Omeprazole (po)	Fluoxetine (po)	40 mg SD on day 6	25 mg BID for 6 days	6	22-28 years; 16.7% F, Japanese, EM	2.73	5.07	3.48	5.34	Yasui-Furukori et al., 2004	<a href="https://pubmed.ncbi.nlm.nih.gov/15025747/">https://pubmed.ncbi.nlm.nih.gov/15025747/</a>
98	<b>CYP2C19</b>	Omeprazole (po)	Fluoxetine (po)	40 mg SD on day 6	25 mg BID for 6 days	6	22-28 years; 16.7% F, Japanese, IM	2.23	3.68	1.91	2.26	Yasui-Furukori et al., 2004	<a href="https://pubmed.ncbi.nlm.nih.gov/15025747/">https://pubmed.ncbi.nlm.nih.gov/15025747/</a>
99	<b>CYP2C19</b>	Omeprazole (IV)	Voriconazole (po)	20 mg IV (10 min), 0.5 hours after Voriconazole	400 mg (2 doses)	10	22-54 years; 60% F, EM	1.06	3.18	2.08	5.51	Mahmoudi et al., 2021	<a href="https://pubmed.ncbi.nlm.nih.gov/33236774/">https://pubmed.ncbi.nlm.nih.gov/33236774/</a>
100	<b>CYP2C19</b>	Omeprazole (po)	Cimetidine (po)	20 mg SD day 6	600 mg BID for 6 days	24	20-27 years; 0 F	-	1.79	-	1.82	Miura et al., 2021	<a href="https://pubmed.ncbi.nlm.nih.gov/33393430/">https://pubmed.ncbi.nlm.nih.gov/33393430/</a>
101	<b>CYP2C19</b>	Omeprazole (po)	Fluconazole (po)	0.1 mg SD day 3	400 mg loading dose day 1, 200 mg QD for 4 days	20	20-27 years; 75% F	2.94	5.83	3.03	12.99	Elbe et al., 2022	<a href="https://pubmed.ncbi.nlm.nih.gov/35238961/">https://pubmed.ncbi.nlm.nih.gov/35238961/</a>

102	<b>CYP2C19</b>	Omeprazole (po)	Fluconazole (po)	20 mg SD day 5	400 mg loading dose day 1, 200 mg QD for 4 days	20	20-27 years; 75% F	2.97	6.21	3.26	8.22	Elbe et al., 2022	<a href="https://pubmed.ncbi.nlm.nih.gov/35238961/">https://pubmed.ncbi.nlm.nih.gov/35238961/</a>
103	<b>CYP2C19</b>	Omeprazole (po)	Fluvoxamine (po)	20 mg SD day 3	25 mg QD for 3 days	15	21-30 years; 0 F, Japanese, non-PM	2.33	3.88	1.91	2.73	Kamiya et al., 2019	<a href="https://pubmed.ncbi.nlm.nih.gov/35238961/">https://pubmed.ncbi.nlm.nih.gov/35238961/</a>
104	<b>CYP2C19</b>	Omeprazole (po)	Fluvoxamine (po)	20 mg SD day 3	25 mg QD for 3 days	15	21-30 years; 0 F, Japanese	2	3.05	1.7	2.26	Kamiya et al., 2019	<a href="https://pubmed.ncbi.nlm.nih.gov/35238961/">https://pubmed.ncbi.nlm.nih.gov/35238961/</a>
105	<b>CYP2C19</b>	Voriconazole (po)	Omeprazole (po)	400 mg BID day 1, 200 mg BID days 2-9, single 200 mg day 10	Omeprazole 40mg QD days 1-10	18	20-40 years; 0 F	2.06	2.8	1.15	1.41	Wood et al., 2003	<a href="https://pubmed.ncbi.nlm.nih.gov/14616415/">https://pubmed.ncbi.nlm.nih.gov/14616415/</a>
106	<b>CYP2C19</b>	Voriconazole (po)	Cimetidine (po)	200mg BID	Cimetidine 400 mg BID	12	21-39 years; 0 F	1.16	1.2	1.18	1.23	Purkins et al., 2003	<a href="https://pubmed.ncbi.nlm.nih.gov/14616414/">https://pubmed.ncbi.nlm.nih.gov/14616414/</a>
107	<b>CYP2C19</b>	Voriconazole (po)	Fluconazole (po)	Loading dose 400 mg BID day 1, 200 mg BID days 2-3, 200mg SD day 4	400 mg SD loading dose day 1, 200 mg QD days 2-5	8	22-43 years; 0F, Japanese	2.02	4.57	1.57	2.5	Damle et al., 2011	<a href="https://pubmed.ncbi.nlm.nih.gov/21876043/">https://pubmed.ncbi.nlm.nih.gov/21876043/</a>
108	<b>CYP2C19</b>	Lansoprazole	Fluoxetine	Lansoprazole, 40 mg SD on day 6	Fluoxetine, 25 mg BID (12 doses)	6	21-29 years; 50% F, Japanese	1.68	4.43	1.54	3.83	Yasui-Furukori et al., 2004	<a href="https://pubmed.ncbi.nlm.nih.gov/15496639/">https://pubmed.ncbi.nlm.nih.gov/15496639/</a>
109	<b>CYP2C19</b>	Lansoprazole	Fluoxetine	Lansoprazole, 40 mg SD on day 6	Fluoxetine, 25 mg BID (12 doses)	6	21-29 years; 50% F, Japanese	1.48	3.6	1.21	2.5	Yasui-Furukori et al., 2004	<a href="https://pubmed.ncbi.nlm.nih.gov/15496639/">https://pubmed.ncbi.nlm.nih.gov/15496639/</a>
110	<b>CYP2D6</b>	Atomoxetine (po)	Fluvoxamine (po)	25 mg Day 6	50 mg QD days 1-3, 100 mg QD days 4-6	18	18-55 years; 50% F	1.27	1.47	1.25	1.33	Todor et al., 2017	<a href="https://pubmed.ncbi.nlm.nih.gov/27816979/">https://pubmed.ncbi.nlm.nih.gov/27816979/</a>
111	<b>CYP2D6</b>	Atomoxetine (po)	Paroxetine (po)	25 mg Day 6	20 mg BID Days 1-2, 20 mg QD days 3-6	22	20-30 years; 32% F, EM/UM	1.6	5.6	1.68	5.79	Todor et al., 2015	<a href="https://pubmed.ncbi.nlm.nih.gov/26733750/">https://pubmed.ncbi.nlm.nih.gov/26733750/</a>
112	<b>CYP2D6</b>	Atomoxetine (po)	Paroxetine (po)	20 mg BID from day 12 (11 doses)	20 mg QD for 17 days	14	20-49 years; 23% F, EM/UM	3.25	5.49	3.52	6.5	Belle et al., 2002	<a href="https://pubmed.ncbi.nlm.nih.gov/12412820/">https://pubmed.ncbi.nlm.nih.gov/12412820/</a>

113	<b>CYP2D6</b>	Atomoxetine (po)	Paroxetine (po)	50 mg on Day 6	20 mg QD for 9 days	20	22-48 years; 15% F, EM/PM (19/1)	1.76	4.71	1.9	5.19	Nichols et al., 2009	<a href="https://pubmed.ncbi.nlm.nih.gov/19001559/">https://pubmed.ncbi.nlm.nih.gov/19001559/</a>
114	<b>CYP2D6</b>	Desipramine (po)	Paroxetine (po)	100 mg on Day 11 (8 am)	20 mg QD for 20 days (8 am)	9	20-24 years; 0 F, EM	1.91	6.51	2.26	6.57	Brosen et al., 1993	<a href="https://pubmed.ncbi.nlm.nih.gov/8513845/">https://pubmed.ncbi.nlm.nih.gov/8513845/</a>
115	<b>CYP2D6</b>	Desipramine (po)	Paroxetine (po)	50 mg QD for 20 days	20 mg QD days 8-17, 30 mg QD days 18-20	17	22-39 years; 0 F, EM/UM	5.29	6.36	4.68	5.46	Alderman et al., 1997	<a href="https://pubmed.ncbi.nlm.nih.gov/9241008/">https://pubmed.ncbi.nlm.nih.gov/9241008/</a>
116	<b>CYP2D6</b>	Desipramine (po)	Fluoxetine (po)	50 mg (3 hours after Fluoxetine)	60 mg Day 1	6	35-53 years, 0 F	1.56	2.39	1.63	2.25	Bergstrom et al., 1992	<a href="https://pubmed.ncbi.nlm.nih.gov/1544284/">https://pubmed.ncbi.nlm.nih.gov/1544284/</a>
117	<b>CYP2D6</b>	Desipramine (po)	Fluoxetine (po)	50 mg on Day 8 (3 hours after Fluoxetine)	60 mg QD for 8 Days	6	35-53 years, 0 F	2.09	5.27	2.54	7.43	Bergstrom et al., 1992	<a href="https://pubmed.ncbi.nlm.nih.gov/1544284/">https://pubmed.ncbi.nlm.nih.gov/1544284/</a>
118	<b>CYP2D6</b>	Desipramine (po)	Fluoxetine (po)	50 mg QD for 28 Days	20 mg QD Days 8-28	9	2-50 years; 0 F, EM/UM	3.99	4.6	4	4.8	Preskorn et al., 1994	<a href="https://pubmed.ncbi.nlm.nih.gov/8195463/">https://pubmed.ncbi.nlm.nih.gov/8195463/</a>
119	<b>CYP2D6</b>	Desipramine (po)	Cinacalcet (po)	50 mg on Day 5	90 mg QD for 7 days	14	18-55 years; 47% F, EM	1.94	2.43	1.71	2.5	Harris et al., 2007	<a href="https://pubmed.ncbi.nlm.nih.gov/16680561/">https://pubmed.ncbi.nlm.nih.gov/16680561/</a>
120	<b>CYP2D6</b>	Desipramine (po)	Bupropion (po)	50 mg on Day 15	150 mg QD days 1-3, 150 mg BID days 4-14, 150 mg SD Day 15	15	20-50 years; 0 F, EM	2.15	4.94	1.89	5.21	Reese et al., 2008	<a href="https://pubmed.ncbi.nlm.nih.gov/18420781/">https://pubmed.ncbi.nlm.nih.gov/18420781/</a>
121	<b>CYP2D6</b>	Dextromethorphan (po)	Quinidine (po)	30 mg SD	50 mg (1 hour before dextromethorphan)	22	18-45; 45% F, EM	4.4	5.86	4.38	7.31	Manap et al., 1999	<a href="https://pubmed.ncbi.nlm.nih.gov/10510150/">https://pubmed.ncbi.nlm.nih.gov/10510150/</a>
122	<b>CYP2D6</b>	Dextromethorphan (po)	Quinidine (po)	30 mg SD	50 mg (1 hour before dextromethorphan)	6	20-26 years; 33% F, EM	4.21	5.57	6.1	6.34	Capon et al., 1996	<a href="https://pubmed.ncbi.nlm.nih.gov/8841152/">https://pubmed.ncbi.nlm.nih.gov/8841152/</a>
123	<b>CYP2D6</b>	Dextromethorphan (po)	Fluoxetine (po)	30 mg on Day 12	20 mg SD Day 1, 60mg QD days 2-14 (1 hour before dextromethorphan)	10	20-40 years; 50% F, EM	4.94	13.8	-	27.21	Sager et al., 2014	<a href="https://pubmed.ncbi.nlm.nih.gov/24569517/">https://pubmed.ncbi.nlm.nih.gov/24569517/</a>
124	<b>CYP2D6</b>	Metoprolol (po)	Paroxetine (po)	100 mg BID on Day 7	20 mg QD for 6 days	15	21-45 years; 26.7%, EM	2.35	3.19	2.2	3.43	Parker et al., 2011	<a href="https://pubmed.ncbi.nlm.nih.gov/21923449/">https://pubmed.ncbi.nlm.nih.gov/21923449/</a>

125	<b>CYP2D6</b>	Metoprolol (po)	Paroxetine (po)	100 mg on Day 7	10 mg every 12 hours for 7 days (13 doses)	8	20-29 years; 0 F, EM/UM	2.03	4.88	2.21	6.16	Hemeryck et al., 2000	<a href="https://pubmed.ncbi.nlm.nih.gov/10741632/">https://pubmed.ncbi.nlm.nih.gov/10741632/</a>
126	<b>CYP2D6</b>	Metoprolol (po)	Quinidine (po)	200 mg on Day 4 (2 hours after Quinidine)	100 mg QD for 5 days	10	24-36 years; EM/UM	2.32	4.59	-	4.89	Johnson et al., 1996	<a href="https://pubmed.ncbi.nlm.nih.gov/8820427/">https://pubmed.ncbi.nlm.nih.gov/8820427/</a>
127	<b>CYP2D6</b>	Metoprolol (IV)	Quinidine (po)	20mg IV infusion	50 mg SD (12 hours before metoprolol)	3	22-34 years; 0 F, EM/UM	1.01	1.46	-	2.35	Leeman et al., 1993	<a href="https://pubmed.ncbi.nlm.nih.gov/8405032/">https://pubmed.ncbi.nlm.nih.gov/8405032/</a>
128	<b>CYP2D6</b>	Nebivolol (po)	Paroxetine (po)	5 mg on Day 8	20 mg BID Days 1-2, 20mg QD days 3-7	23	20-35 years; 30% F	3.72	7.28	2.38	6.96	Briciu et al., 2014	<a href="https://pubmed.ncbi.nlm.nih.gov/24845234/">https://pubmed.ncbi.nlm.nih.gov/24845234/</a>
129	<b>CYP2D6</b>	Nebivolol (po)	Bupropion (po)	5 mg on Day 8	150 mg BID days 1-3, 300 mg days 4-7	18	20-30 years; 44% F, EM/UM	4.45	8.58	2.28	6.98	Gheldiu et al., 2016	<a href="https://pubmed.ncbi.nlm.nih.gov/27300331/">https://pubmed.ncbi.nlm.nih.gov/27300331/</a>
130	<b>CYP2D6</b>	Nebivolol (po)	Fluvoxamine (po)	5 mg on Day 8	50 mg QD days 1-3, 100 mg QD days 3-7	18	20-30 years; 44% F, EM/UM	1.67	1.61	1.32	1.57	Gheldiu et al., 2017	<a href="https://pubmed.ncbi.nlm.nih.gov/28459657/">https://pubmed.ncbi.nlm.nih.gov/28459657/</a>
131	<b>CYP2D6</b>	Nebivolol (po)	Fluoxetine (po)	10 mg SD on day 21	20 mg QD days 1-21	10	20-52 years; 0 F, EM	3.38	5.87	2.39	6.92	Lindamood et al., 2011	<a href="https://pubmed.ncbi.nlm.nih.gov/20489028/">https://pubmed.ncbi.nlm.nih.gov/20489028/</a>
132	<b>CYP2D6</b>	Tolterodine (po)	Fluoxetine (po)	2 mg BID days 22-24 (5 doses)	20 mg QD for 24 days	7	48-78 years; 100% F, EM	3.64	6.49	4.53	7.71	Brynne et al., 1999	<a href="https://pubmed.ncbi.nlm.nih.gov/10583026/">https://pubmed.ncbi.nlm.nih.gov/10583026/</a>
133	<b>CYP2D6</b>	Tolterodine (po)	Fluoxetine (po)	2 mg BID days 22-24 (5 doses)	20 mg QD for 24 days	2	48-78 years; 100% F, PM	1.21	1.29	1.39	1.25	Brynne et al., 1999	<a href="https://pubmed.ncbi.nlm.nih.gov/10583026/">https://pubmed.ncbi.nlm.nih.gov/10583026/</a>
134	<b>CYP2D6</b>	Desipramine (po)	Mirabegron (po)	50 mg SD (day 13)	100 mg once daily for 18 days (18 doses)	28	18-53 years; 50% F, EM	1.58	2.8	1.79	3.41	Krauwinkel et al., 2014	<a href="https://pubmed.ncbi.nlm.nih.gov/23728524/">https://pubmed.ncbi.nlm.nih.gov/23728524/</a>
135	<b>CYP2D6</b>	Propranolol (po)	Quinidine (po)	10 mg SD	100 mg 12h before and simultaneously	5	20-23 years; 0 F, Japanese	-	2.86	-	2.76	Yasuhara et al., 1990	<a href="https://pubmed.ncbi.nlm.nih.gov/2093126/">https://pubmed.ncbi.nlm.nih.gov/2093126/</a>
136	<b>CYP2D6</b>	Propranolol (po)	Quinidine (po)	20 mg SD	200 mg SD	11	20-38 years; 0 F, Japanese	-	3.09	-	2.66	Yasuhara et al., 1990	<a href="https://pubmed.ncbi.nlm.nih.gov/2093126/">https://pubmed.ncbi.nlm.nih.gov/2093126/</a>
137	<b>CYP2D6</b>	Propranolol (po)	Quinidine (po)	80 mg SD	50 mg SD	6	18-42 years; 0 F	-	2.5	-	1.92	Zhou et al., 1990	<a href="https://pubmed.ncbi.nlm.nih.gov/2357863/">https://pubmed.ncbi.nlm.nih.gov/2357863/</a>

138	<b>CYP2D6</b>	Metoprolol (po)	Duloxetine (po)	100 mg SD day 17	30 mg day 1, 60 mg QD days 2-17	16	20-43 years; 48% F, EM	1.23	1.76	1.67	1.94	Preskorn et al., 2007	<a href="https://pubmed.ncbi.nlm.nih.gov/17224709/">https://pubmed.ncbi.nlm.nih.gov/17224709/</a>
139	<b>CYP2D6</b>	Dextromethorphan (po)	Fluvoxamine (po)	30 mg SD day 2	18.3 mg free base BID 3 doses	24	20-27 years; 0 F	-	1.32	-	1.33	Miura et al., 2021	<a href="https://pubmed.ncbi.nlm.nih.gov/33393430/">https://pubmed.ncbi.nlm.nih.gov/33393430/</a>
140	<b>CYP2D6</b>	Propranolol (po)	Cimetidine (po)	20 mg SD	400mg TID (10 doses)	6	23-32 years; 0 F, Japanese	2.01	2.06	2.02	1.89	Tateishi et al., 1992	<a href="https://pubmed.ncbi.nlm.nih.gov/1487547/">https://pubmed.ncbi.nlm.nih.gov/1487547/</a>
141	<b>CYP2D6</b>	Propranolol (po)	Cimetidine (po)	80 mg BID 7 days	200 mg TID 7 days	6	22-31 years; 0 F	1.7	1.73	1.99	1.91	Kirch et al., 1982	<a href="https://pubmed.ncbi.nlm.nih.gov/6115283/">https://pubmed.ncbi.nlm.nih.gov/6115283/</a>
142	<b>CYP2D6</b>	Propranolol (po)	Cimetidine (po)	80 mg SD	300 mg QID 2 days before and on the day	12	18-30 years; 0 F	1.85	2.02	1.35	1.46	Duchin et al., 1984	<a href="https://pubmed.ncbi.nlm.nih.gov/6148867/">https://pubmed.ncbi.nlm.nih.gov/6148867/</a>
143	<b>CYP2D6</b>	Desipramine (po)	Paroxetine (po)	100 mg on Day 8 (8 am)	20 mg QD for 8 days (8 am)	15	27-54 years; 47% F, EM	1.85	3.89	2.03	4.84	Laine et al., 2003	<a href="https://pubmed.ncbi.nlm.nih.gov/14730412/">https://pubmed.ncbi.nlm.nih.gov/14730412/</a>
144	<b>CYP2D6</b>	Desipramine (po)	Cimetidine (po)	500 mg on Day 5 (8 am)	400 mg TID for 5 days (8 am)	5	25-38; 40% F, EM	-	1.68	-	1.78	Steiner et al., 1987	<a href="https://pubmed.ncbi.nlm.nih.gov/3621781/">https://pubmed.ncbi.nlm.nih.gov/3621781/</a>
145	<b>CYP2D6</b>	Metoprolol (po)	Cimetidine (po)	100 mg SD day 8	800 mg QD for 8 days	12	19-35 years; 50% F	1.89	2.16	1.63	1.62	Chellingsworth et al., 1988	<a href="https://pubmed.ncbi.nlm.nih.gov/2979275/">https://pubmed.ncbi.nlm.nih.gov/2979275/</a>
146	<b>CYP2D6</b>	Paroxetine (po)	Cimetidine (po)	30 mg on day 8	200 mg QID for 8 days	10	20-28 years; 0 F	1.64	2.07	1.01	1.17	Greg et al., 1989	<a href="https://pubmed.ncbi.nlm.nih.gov/2530801/">https://pubmed.ncbi.nlm.nih.gov/2530801/</a>
147	<b>CYP2D6</b>	Metoprolol (po)	Cimetidine (po)	100 mg BID for 8 days (15 doses)	800 mg QD for 8 days	12	19-32 years; 50% F	1.85	2.08	1.51	1.56	Chellingsworth et al., 1988	<a href="https://pubmed.ncbi.nlm.nih.gov/2979275/">https://pubmed.ncbi.nlm.nih.gov/2979275/</a>
148	<b>CYP2D6</b>	Paroxetine (po)	Cimetidine (po)	30 mg MD for 28 days	300 mg TID from day 22 to 28	11	20-50 years; 0 F	1.27	1.32	1.45	1.51	Bannister et al., 1989	<a href="https://pubmed.ncbi.nlm.nih.gov/2530759/">https://pubmed.ncbi.nlm.nih.gov/2530759/</a>
149	<b>CYP2D6</b>	Nebivolol (po)	Cimetidine (po)	5 mg (4.59 free base) SD day 2	300 mg BID 24h before and 48h after neбиволol administration	12	19-23 years; 0 F, EM	2.27	2.11	1.23	1.48	Kamali et al., 1997	<a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2042729/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2042729/</a>
150	<b>CYP2D6</b>	Metoprolol (po)	Cimetidine (po)	100 mg BID	200 mg TID 7 days	6	22-31 years; 0 F	1.59	1.71	1.6	1.62	Kirch et al., 1982	<a href="https://pubmed.ncbi.nlm.nih.gov/6115283/">https://pubmed.ncbi.nlm.nih.gov/6115283/</a>
151	<b>CYP2D6</b>	Tolterodine (po)	Duloxetine (po)	1.368 mg free base BID 9 doses	40 mg BID 9 doses	14	21-54 years; 79% F	1.74	2.22	1.64	1.71	Hua et al., 2004	<a href="https://pubmed.ncbi.nlm.nih.gov/15089819/">https://pubmed.ncbi.nlm.nih.gov/15089819/</a>

152	<b>CYP2D6</b>	Nebivolol (po)	Duloxetine (po)	5 mg (4.59 mg free base) SD day 4	30 mg BID for 2 days, then QD for 2 days	23	20-33 years; 0 F, Japanese	1.44	1.7	1.1	1.29	Briciu et al., 2014	<a href="https://researchgate.net/publication/271271833_A_pharmacokinetic_drug_interaction_study_between_nebivolol_and_duloxetine">https://researchgate.net/publication/271271833_A_pharmacokinetic_drug_interaction_study_between_nebivolol_and_duloxetine</a>
153	<b>CYP2D6</b>	Dextromethorphan (po)	Cinacalcet (po)	30 mg SD	50 mg MD (8 doses)	23	20-35 years; 50% F	3.66	4.51	4.06	4.93	Nakashima et al., 2007	<a href="https://pubmed.ncbi.nlm.nih.gov/17652181">https://pubmed.ncbi.nlm.nih.gov/17652181</a>
154	<b>CYP3A4</b>	Alfentanil (IV)	Fluconazole (po)	15 µg/kg IV (3 hr after fluconazole)	100 mg SD	12	19-36 years; 50% F	-	1.27	-	1.20	Kharasch et al., 2005	<a href="https://pubmed.ncbi.nlm.nih.gov/16172184/">https://pubmed.ncbi.nlm.nih.gov/16172184/</a>
155	<b>CYP3A4</b>	Alfentanil (po)	Fluconazole (po)	40 µg/kg (3 hr after fluconazole)	100 mg SD	12	19-36 years; 50% F	1.42	1.67	1.16	1.80	Kharasch et al., 2005	<a href="https://pubmed.ncbi.nlm.nih.gov/16172184/">https://pubmed.ncbi.nlm.nih.gov/16172184/</a>
156	<b>CYP3A4</b>	Alfentanil (IV)	Fluconazole (po)	15 µg/kg IV (3 hr after fluconazole)	200 mg SD	12	19-36 years; 50% F	-	1.51	-	1.6	Kharasch et al., 2005	<a href="https://pubmed.ncbi.nlm.nih.gov/16172184/">https://pubmed.ncbi.nlm.nih.gov/16172184/</a>
157	<b>CYP3A4</b>	Alfentanil (po)	Fluconazole (po)	40 µg/kg (3 hr after fluconazole)	200 mg SD	12	19-36 years; 50% F	1.76	2.32	1.53	2.9	Kharasch et al., 2005	<a href="https://pubmed.ncbi.nlm.nih.gov/16172184/">https://pubmed.ncbi.nlm.nih.gov/16172184/</a>
158	<b>CYP3A4</b>	Alfentanil (IV)	Fluconazole (po)	15 µg/kg IV (3 hr after fluconazole)	400 mg SD	12	19-36 years; 50% F	-	1.94	-	2.2	Kharasch et al., 2005	<a href="https://pubmed.ncbi.nlm.nih.gov/16172184/">https://pubmed.ncbi.nlm.nih.gov/16172184/</a>
159	<b>CYP3A4</b>	Alfentanil (po)	Fluconazole (po)	40 µg/kg (3 hr after fluconazole)	400 mg SD	12	19-36 years; 50% F	2.25	3.55	1.72	4.9	Kharasch et al., 2005	<a href="https://pubmed.ncbi.nlm.nih.gov/16172184/">https://pubmed.ncbi.nlm.nih.gov/16172184/</a>
160	<b>CYP3A4</b>	Alfentanil (IV)	Ketoconazole (po)	0.5 mg IV on day 4 (assuming at 7:00 AM)	400 mg for 3 days (3 doses at 11:30 PM)	6	21-33 years; 50% F	-	3.96	-	4.8	Kharasch et al., 2011	<a href="https://pubmed.ncbi.nlm.nih.gov/21346758/">https://pubmed.ncbi.nlm.nih.gov/21346758/</a>
161	<b>CYP3A4</b>	Alfentanil (po)	Ketoconazole (po)	1 mg on day 4 (10:00 AM)	400 mg for 3 days (3 doses at 11:30 PM)	6	21-33 years; 50% F	3.47	7.25	2.75	9.20	Kharasch et al., 2011	<a href="https://pubmed.ncbi.nlm.nih.gov/21346758/">https://pubmed.ncbi.nlm.nih.gov/21346758/</a>
162	<b>CYP3A4</b>	Alfentanil (IV)	Ketoconazole (po)	0.5 mg IV on day 5 (7:00 AM)	400 mg for 4 days (4 doses at 11:30 PM)	6	21-33 years; 50% F	-	3.88	-	5.00	Kharasch et al., 2011	<a href="https://pubmed.ncbi.nlm.nih.gov/21346758/">https://pubmed.ncbi.nlm.nih.gov/21346758/</a>
163	<b>CYP3A4</b>	Alfentanil (po)	Ketoconazole (po)	1 mg on day 5 (7:00 AM)	400 mg for 4 days (4 doses at 11:30 PM)	6	21-33 years; 50% F	3.93	9.9	5.07	12.00	Kharasch et al., 2011	<a href="https://pubmed.ncbi.nlm.nih.gov/21346758/">https://pubmed.ncbi.nlm.nih.gov/21346758/</a>

164	<b>CYP3A4</b>	Alprazolam (po)	Ketoconazole (po)	1 mg on day 3 (1 h after 5th Ketoconazole dose)	200 mg BID for 4 days (8 doses)	7	21-44 years; 0 F	1.1	2.75	1.1	3.98	Greenblatt et al., 1988	<a href="https://pubmed.ncbi.nlm.nih.gov/9757147/">https://pubmed.ncbi.nlm.nih.gov/9757147/</a>
165	<b>CYP3A4</b>	Alprazolam (po)	Ketoconazole (po)	0.5 mg on day 4	200 mg BID for 6 days (12 doses)	8	18-38 years; 0 F	1.09	2.92	1.19	2.89	Boulenc et al., 2016	<a href="https://pubmed.ncbi.nlm.nih.gov/25374256/">https://pubmed.ncbi.nlm.nih.gov/25374256/</a>
166	<b>CYP3A4</b>	Alprazolam (po)	Ketoconazole (po)	0.5 mg on day 4	400 mg QD for 6 days (6 doses)	8	18-38 years; 0 F	1.09	2.57	1.18	2.7	Boulenc et al., 2016	<a href="https://pubmed.ncbi.nlm.nih.gov/25374256/">https://pubmed.ncbi.nlm.nih.gov/25374256/</a>
167	<b>CYP3A4</b>	Alprazolam (po)	Erythromycin (po)	0.8 mg on day 8	400 mg TID for 10 days (30 doses)	12	25-41 years; 0 F, Japanese	1.07	2.49	1.18	2.47	Yasui et al., 1996	<a href="https://pubmed.ncbi.nlm.nih.gov/8646822/">https://pubmed.ncbi.nlm.nih.gov/8646822/</a>
168	<b>CYP3A4</b>	Alprazolam (po)	Fluoxetine (po)	1 mg on day 22	20 mg QD for 24 days	11	20-40 years; 50% F	1.02	1.23	1.09	1.32	Hall et al., 2003	<a href="https://pubmed.ncbi.nlm.nih.gov/12920410/">https://pubmed.ncbi.nlm.nih.gov/12920410/</a>
169	<b>CYP3A4</b>	Alprazolam (po)	Cimetidine (po)	0.5 mg TID for 7 days and morning dose on day 8	200 mg TID with 400 mg at night for 9 days	8	21-26 years; 50% F	1.13	1.31	1.82	1.73	Pourbaix et al., 1985	<a href="https://pubmed.ncbi.nlm.nih.gov/2864320/">https://pubmed.ncbi.nlm.nih.gov/2864320/</a>
170	<b>CYP3A4</b>	Aprepitant (po)	Ketoconazole (po)	125 mg SD day 5	400 mg QD for 10 days	10	20-50 years; 50% F	1.48	4.02	1.52	4.78	CDER Clinical Pharmacology and Biopharmaceutics Reviews Application Number 21-549, 2003	<a href="https://www.accessdata.fda.gov/drugsatfda_docs/nda/2003/21-549_Emend_biopharmr.pdf">https://www.accessdata.fda.gov/drugsatfda_docs/nda/2003/21-549_Emend_biopharmr.pdf</a>
171	<b>CYP3A4</b>	Atazanavir (po)	Ketoconazole (po)	400 mg QD for 13 days	200 mg QD days 7 – 13	15	20-50 years; 0 F	1.17	1.21	0.98	1.10	O'Mara et al., 2000	N/A
172	<b>CYP3A4</b>	Atazanavir (po)	Clarithromycin (po)	400 mg QD for 10 days	500mg BID days 7 – 10	30	20-50 years; 50% F	1.08	1.10	1.06	1.28	Mummaneini et al., 2002	N/A
173	<b>CYP3A4</b>	Clarithromycin (po)	Atazanavir (po)	500 mg BID days 7 – 10	400 mg QD for 10 days	30	20-50 years; 50% F	1.37	1.59	1.50	1.94	Mummaneini et al., 2002	N/A
174	<b>CYP3A4</b>	Dexamethasone (po)	Itraconazole (po)	4.5 mg Day 4 at 9am	200 mg QD at 7.30 am on day 1-3 and 8am on day 4	8	20-42 years; 88% F	1.59	3.55	1.58	3.69	Varis et al., 2000	<a href="https://pubmed.ncbi.nlm.nih.gov/11103751/">https://pubmed.ncbi.nlm.nih.gov/11103751/</a>

175	<b>CYP3A4</b>	Ibrutinib (po)	Ketoconazole (po)	120 mg on Day 4 at 10 am	400 mg QD Days 1-6 at 9 am	18	18-55 years; 0 F	17.97	25.48	28.6	26.2	de Jong et al., 2015	<a href="https://pubmed.ncbi.nlm.nih.gov/26171235/">https://pubmed.ncbi.nlm.nih.gov/26171235/</a>
176	<b>CYP3A4</b>	Ibrutinib (po)	Itraconazole (po)	140 mg on Day 3 at 9 am (low fat fed)	200 mg BID Day 1 (8 am and 8 pm) and QD Days 2-3 (8 am)	11	19-38 years; 0 F	9.48	13.11	8.8	9.99	Tapaninen et al., 2020	<a href="https://pubmed.ncbi.nlm.nih.gov/31664782/">https://pubmed.ncbi.nlm.nih.gov/31664782/</a>
177	<b>CYP3A4</b>	Midazolam (po)	Fluconazole (po)	7.5 mg (1 h after Fluconazole)	400 mg SD	9	19-25 years; 44% F	1.91	3.03	2.3	3.73	Ahonen et al., 1997	<a href="https://pubmed.ncbi.nlm.nih.gov/9049584">https://pubmed.ncbi.nlm.nih.gov/9049584</a>
178	<b>CYP3A4</b>	Midazolam (po)	Itraconazole (po)	7.5 mg (day 4)	200 mg QD for 4 days (8 doses)	9	19-26; 77% F	2.82	9.97	3.41	10.77	Olkkola et al., 1994	<a href="https://pubmed.ncbi.nlm.nih.gov/8181191">https://pubmed.ncbi.nlm.nih.gov/8181191</a>
179	<b>CYP3A4</b>	Midazolam (po)	Clarithromycin (po)	15 mg SD (day 5)	250 mg BID for 5 days (10 doses)	12	24-53 years; 67% F	2.07	4.14	2.44	3.57	Yeates et al., 1996	<a href="https://pubmed.ncbi.nlm.nih.gov/8880291">https://pubmed.ncbi.nlm.nih.gov/8880291</a>
180	<b>CYP3A4</b>	Midazolam (po)	Diltiazem (po)	15 mg on day 2 (1 h after 4th Diltiazem dose)	60 mg TID for 2 days (5 doses)	9	19-28 years; 0 F	1.55	2.04	2.05	3.75	Backman et al., 1994	<a href="https://pmc.ncbi.nlm.nih.gov/articles/PMC1364750/">https://pmc.ncbi.nlm.nih.gov/articles/PMC1364750/</a>
181	<b>CYP3A4</b>	Midazolam (po)	Verapamil (po)	15 mg on day 2 (1 h after 4th Verapamil dose)	80 mg TID for 2 days (5 doses)	9	19-28 years; 0 F	2.07	3.39	1.97	2.92	Backman et al., 1994	<a href="https://pmc.ncbi.nlm.nih.gov/articles/PMC1364750/">https://pmc.ncbi.nlm.nih.gov/articles/PMC1364750/</a>
182	<b>CYP3A4</b>	Midazolam (po)	Ketoconazole (po)	6 mg (12 h after 1st Ketoconazole dose)	200 mg BID for 2 days (3 doses)	9	19-41 years; 33% F	3.56	12.56	4.24	13.62	Tsunoda et al., 1999	<a href="https://pubmed.ncbi.nlm.nih.gov/10579473/">https://pubmed.ncbi.nlm.nih.gov/10579473/</a>
183	<b>CYP3A4</b>	Midazolam (IV)	Ketoconazole (po)	2 mg IV (12 h after 1st Ketoconazole dose)	200 mg BID for 2 days (3 doses)	9	19-41 years; 33% F	-	4.69	-	5.04	Tsunoda et al., 1999	<a href="https://pubmed.ncbi.nlm.nih.gov/10579473/">https://pubmed.ncbi.nlm.nih.gov/10579473/</a>
184	<b>CYP3A4</b>	Midazolam (po)	Ketoconazole (po)	7.5 mg on day 4	400 mg QD for 4 days (4 doses)	9	19-26 years; 77% F	3.78	12.51	4.09	15.9	Olkkola et al., 1994	<a href="https://pubmed.ncbi.nlm.nih.gov/8181191">https://pubmed.ncbi.nlm.nih.gov/8181191</a>
185	<b>CYP3A4</b>	Midazolam (po)	Ketoconazole (po)	2 mg on day 5	400 mg QD for 5 days (5 doses)	10	21-54 years; 0 F	3.76	12.13	5.42	13.96	Stoch et al., 2009	<a href="https://pubmed.ncbi.nlm.nih.gov/19246722/">https://pubmed.ncbi.nlm.nih.gov/19246722/</a>
186	<b>CYP3A4</b>	Midazolam (po)	Cimetidine (po)	15 mg on Day 2 (30 min after cimetidine)	400 mg BID (3 doses)	8	22-40 years; 12.5%	-	1.74	-	1.35	Fee et al., 1987	<a href="https://pubmed.ncbi.nlm.nih.gov/3802710/">https://pubmed.ncbi.nlm.nih.gov/3802710/</a>

187	<b>CYP3A4</b>	Midazolam (po)	Cimetidine (po)	15 mg (2hrs after cimetidine)	400 mg SD	6	24-38 years; 50% F	1.42	1.51	1.37	1.36	Salonen et al., 1986	<a href="https://pubmed.ncbi.nlm.nih.gov/2939688/">https://pubmed.ncbi.nlm.nih.gov/2939688/</a>
188	<b>CYP3A4</b>	Midazolam (po)	Cimetidine (po)	15 mg on day 2 (2.5hr after cimetidine)	200 mg TID with 400 mg at night on day 1, 200 mg on day 2	5	29-54 years; 0 F	1.19	1.22	2.38	2.02	Elliott et al., 1986	<a href="https://pubmed.ncbi.nlm.nih.gov/6152615/">https://pubmed.ncbi.nlm.nih.gov/6152615/</a>
189	<b>CYP3A4</b>	Midazolam (po)	Erythromycin (po)	15 mg on day 6	Erythromycin, 500 mg TID 7 days	12	18-29 years; 75%	3.01	8.73	2.7	4.42	Oikkola et al., 1993	<a href="https://pubmed.ncbi.nlm.nih.gov/8453848/">https://pubmed.ncbi.nlm.nih.gov/8453848/</a>
190	<b>CYP3A4</b>	Midazolam (po)	Fluvoxamine (po)	10 mg on day 12 (1h after fluvoxamine)	50 mg BID days 1-6, 100 mg (73.3 mg free base) BID days 7-12	10	18-50 years; 57% F	1.25	1.37	1.38	1.39	Lam et al., 2003	<a href="https://pubmed.ncbi.nlm.nih.gov/1451182/">https://pubmed.ncbi.nlm.nih.gov/1451182/</a>
191	<b>CYP3A4</b>	Midazolam (po)	Itraconazole (po)	7.5 mg on day 4	100 mg QD for 4 days	12	19-30 years; 66% F	2.38	4.99	2.56	5.75	Ahonen et al., 1995	<a href="https://pubmed.ncbi.nlm.nih.gov/8527290/">https://pubmed.ncbi.nlm.nih.gov/8527290/</a>
192	<b>CYP3A4</b>	Midazolam (po)	Itraconazole (po)	7.5 mg on day 4	200 mg QD for 4 days	9	22-34 years; 55% F	2.82	7.15	2.91	6.16	Backman et al., 1998	<a href="https://pubmed.ncbi.nlm.nih.gov/9591931/">https://pubmed.ncbi.nlm.nih.gov/9591931/</a>
193	<b>CYP3A4</b>	Midazolam (po)	Ketoconazole (po)	2 mg, 5 min after ketoconazole dosing	400 mg SD	10	21-54 years; 0 F	4.07	13.34	5.01	10.31	Stoch et al., 2009	<a href="https://pubmed.ncbi.nlm.nih.gov/19246722/">https://pubmed.ncbi.nlm.nih.gov/19246722/</a>
194	<b>CYP3A4</b>	Midazolam (po)	Ketoconazole (po)	75 ug on day 3	200 mg BID 2 days	4	23-55 years; 38% F	2.56	4.9	3.74	6.47	Eap et al., 2004	<a href="https://pubmed.ncbi.nlm.nih.gov/15114429/">https://pubmed.ncbi.nlm.nih.gov/15114429/</a>
195	<b>CYP3A4</b>	Nifedipine (po)	Cimetidine (po)	10 mg TID for 4 days, 1 dose day 5	800 mg QD for 5 days	17	19-35 years; 0 F	1.52	2	2.3	2.01	Khan et al., 1991	<a href="https://pubmed.ncbi.nlm.nih.gov/1958451/">https://pubmed.ncbi.nlm.nih.gov/1958451/</a>
196	<b>CYP3A4</b>	Nifedipine (po)	Cimetidine (po)	10 mg QID for 6 days, 1 dose day 7	200 mg TID with 400 mg at night for 7 days	6	25-35 years; 50% F	1.26	1.5	2.02	1.6	Kirch et al., 1984	<a href="https://pubmed.ncbi.nlm.nih.gov/6151387/">https://pubmed.ncbi.nlm.nih.gov/6151387/</a>
197	<b>CYP3A4</b>	Nifedipine (po)	Cimetidine (po)	20 mg on day 7	300 mg QID for 7 days	11	20-50 years; 9.1% F	1.39	1.66	1.6	1.8	Schwartz et al., 1988	<a href="https://pubmed.ncbi.nlm.nih.gov/3378388/">https://pubmed.ncbi.nlm.nih.gov/3378388/</a>
198	<b>CYP3A4</b>	Nifedipine (po)	Cimetidine (po)	20 mg on day 5 (1hr after cimetidine)	800 mg QD for 5 days	12	18-40 years; 50% F	1.88	2.32	1.65	1.77	Smith et al., 1987	<a href="https://pubmed.ncbi.nlm.nih.gov/3567045/">https://pubmed.ncbi.nlm.nih.gov/3567045/</a>

199	<b>CYP3A4</b>	Nifedipine (po)	Diltiazem (po)	20 mg SD	60 mg 1 hour before nifedipine	6	23-29 years; 0 F, Japanese	-	1.12	-	1.33	Ohashi et al., 1993	<a href="https://pubmed.ncbi.nlm.nih.gov/8463435/">https://pubmed.ncbi.nlm.nih.gov/8463435/</a>
200	<b>CYP3A4</b>	Nifedipine (po)	Diltiazem (po)	20 mg SD	60 mg TID for 3 days and a final dose 1 hour before nifedipine	6	20-32 years; 0 F, Japanese	-	2.61	-	2.4	Ohashi et al., 1993	<a href="https://pubmed.ncbi.nlm.nih.gov/8463435/">https://pubmed.ncbi.nlm.nih.gov/8463435/</a>
201	<b>CYP3A4</b>	Nifedipine (po)	Diltiazem (po)	20 mg SD	60 mg TID for 6 days and a final dose 1 hour before nifedipine	6	20-22 years; 0 F, Japanese	-	2.82	-	2.96	Ohashi et al., 1993	<a href="https://pubmed.ncbi.nlm.nih.gov/8463435/">https://pubmed.ncbi.nlm.nih.gov/8463435/</a>
202	<b>CYP3A4</b>	Nifedipine (po)	Diltiazem (po)	20 mg SD	30 mg TID for 3 days and a final dose 1 hour before nifedipine	6	20-25 years; 0 F, Japanese	1.41	1.8	2.01	2.22	Tateishi et al., 1989	<a href="https://pubmed.ncbi.nlm.nih.gov/2600195/">https://pubmed.ncbi.nlm.nih.gov/2600195/</a>
203	<b>CYP3A4</b>	Nifedipine (po)	Diltiazem (po)	20 mg SD	90 mg TID for 3 days and a final dose 1 hour before nifedipine	6	20-25 years; 0 F, Japanese	1.84	3.36	1.71	3.11	Tateishi et al., 1989	<a href="https://pubmed.ncbi.nlm.nih.gov/2600195/">https://pubmed.ncbi.nlm.nih.gov/2600195/</a>
204	<b>CYP3A4</b>	Quinidine (po)	Verapamil (po)	332 mg on day 4, 30 min after verapamil	80 mg TID for 4 days (12 doses)	6	23-34 years; 0 F	-	1.55	-	1.47	Edwards et al., 1987	<a href="https://pubmed.ncbi.nlm.nih.gov/3802708/">https://pubmed.ncbi.nlm.nih.gov/3802708/</a>
205	<b>CYP3A4</b>	Quinidine (po)	Verapamil (po)	332 mg on day 4, 30 min after verapamil	120 mg TID for 4 days (12 doses)	6	23-34 years; 0 F	-	1.67	-	1.5	Edwards et al., 1987	<a href="https://pubmed.ncbi.nlm.nih.gov/3802708/">https://pubmed.ncbi.nlm.nih.gov/3802708/</a>
206	<b>CYP3A4</b>	Quinidine (po)	Diltiazem (po)	200 mg on day 3 (1.5 h after last Diltiazem dose)	90 mg BID for 3 days (5 doses)	12	19-37 years; 0 F	1.18	1.65	1.1	1.51	Laganier et al., 1996	<a href="https://pubmed.ncbi.nlm.nih.gov/8841148/">https://pubmed.ncbi.nlm.nih.gov/8841148/</a>
207	<b>CYP3A4</b>	Quinidine (po)	Cimetidine (po)	330 mg (free base) SD on day 6	300 mg QID for 7 days	6	25-38 years; 0 F	1.12	1.3	1.2	1.57	Hardy et al., 1983	<a href="https://pubmed.ncbi.nlm.nih.gov/6858908/">https://pubmed.ncbi.nlm.nih.gov/6858908/</a>
208	<b>CYP3A4</b>	Quinidine (po)	Cimetidine (po)	330 mg (free base) on day 4	300 mg QID for 3 days, morning dose day 4	9	21-35 years; 0 F	1.11	1.17	0.99	1.27	Kolb et al., 1984	<a href="https://pubmed.ncbi.nlm.nih.gov/6506138/">https://pubmed.ncbi.nlm.nih.gov/6506138/</a>
209	<b>CYP3A4</b>	Quinidine (po)	Itraconazole (po)	166 mg free base on day 6	100 mg QD for 7 days	6	20-35 years; 0 F	1.34	2.3	1.32	2.58	Damkier et al., 1999	<a href="https://pubmed.ncbi.nlm.nih.gov/10594487/">https://pubmed.ncbi.nlm.nih.gov/10594487/</a>
210	<b>CYP3A4</b>	Quinidine (po)	Itraconazole (po)	83 mg free base on day 4	200 mg QD for 4 days	9	21-32 years; 56% F	1.37	2.84	1.59	2.42	Kaukonen et al., 1997	<a href="https://pubmed.ncbi.nlm.nih.gov/9390107/">https://pubmed.ncbi.nlm.nih.gov/9390107/</a>

211	<b>CYP3A4</b>	Quinidine (po)	Erythromycin (po)	166 mg free base on day 6	250 mg QID for 7 days	6	20-35 years; 0 F	1.26	2.45	1.39	1.19	Damkier et al., 1999	<a href="https://pubmed.ncbi.nlm.nih.gov/10594487/">https://pubmed.ncbi.nlm.nih.gov/10594487/</a>
212	<b>CYP3A4</b>	Quinidine (po)	Fluvoxamine (po)	166 mg free base on day 5	100 mg QD for 6 days	6	20-35 years; 0 F	1.1	1.22	1.35	1.41	Damkier et al., 1999	<a href="https://pubmed.ncbi.nlm.nih.gov/10492058/">https://pubmed.ncbi.nlm.nih.gov/10492058/</a>
213	<b>CYP3A4</b>	Repaglinide (po)	Itraconazole (po)	0.25 mg on day 3 (1 h after Itraconazole)	200 mg (1st dose) 100 mg BID for 3 days (7 doses)	12	20-24 years; 66% F	1.31	1.51	1.48	1.41	Niemi et al., 2003	<a href="https://pubmed.ncbi.nlm.nih.gov/12687332/">https://pubmed.ncbi.nlm.nih.gov/12687332/</a>
214	<b>CYP3A4</b>	Repaglinide (po)	Clarithromycin (po)	0.25 mg on day 5 given 1 hour after clarithromycin	250 mg BID for 4 days	9	22-27 years; 44% F	1.29	1.44	1.42	1.66	Niemi et al., 2001	<a href="https://pubmed.ncbi.nlm.nih.gov/11452245/">https://pubmed.ncbi.nlm.nih.gov/11452245/</a>
215	<b>CYP3A4</b>	Rifabutin (po)	Fluconazole (po)	300 mg QD for 14 days	200 mg QD for 14 days	10	20-50 years; 50% F	1.29	1.64	1.88	1.82	FDA 2007	<a href="https://cdn.pfizer.com/pfizercom/products/us_pi_mycobutin.pdf">https://cdn.pfizer.com/pfizercom/products/us_pi_mycobutin.pdf</a>
216	<b>CYP3A4</b>	Rifabutin (po)	Fluconazole (po)	300 mg QD from day 15	200 mg QD for 28 days	12	29-43 years; 31% F	-	1.68	-	1.8	Trapnell et al., 1996	<a href="https://pubmed.ncbi.nlm.nih.gov/8597321/">https://pubmed.ncbi.nlm.nih.gov/8597321/</a>
217	<b>CYP3A4</b>	Rifabutin (po)	Clarithromycin (po)	300 mg QD for 42 days	500 mg BD from day 15	16	18-45 years; 6% F	1.45	1.96	5.33	3.04	Hafner et al., 1998	<a href="https://pubmed.ncbi.nlm.nih.gov/9517944/">https://pubmed.ncbi.nlm.nih.gov/9517944/</a>
218	<b>CYP3A4</b>	Sildenafil (po)	Clarithromycin (po)	50 mg (2 h after Clarithromycin dose)	500 mg SD	12	25-39 years; 0F	1.46	1.69	2.42	2.28	Hedeya et al., 2006	<a href="https://pubmed.ncbi.nlm.nih.gov/16372380/">https://pubmed.ncbi.nlm.nih.gov/16372380/</a>
219	<b>CYP3A4</b>	Sildenafil (po)	Erythromycin (po)	100 mg on day 5) (1 h after 10th Erythromycin dose)	500 BID for 5 days (10 doses)	26	18-45 years; 0 F	2.2	4.78	2.09	2.58	Muirhead et al., 2002	<a href="https://pubmed.ncbi.nlm.nih.gov/11879258/">https://pubmed.ncbi.nlm.nih.gov/11879258/</a>
220	<b>CYP3A4</b>	Sildenafil (po)	Cimetidine (po)	50 mg on day 3 (2hrs after cimetidine)	800 mg QD for 4 days	10	18-39 years; 0 F	1.63	1.77	1.35	1.41	Wilner et al., 2002	<a href="https://pubmed.ncbi.nlm.nih.gov/11879257/">https://pubmed.ncbi.nlm.nih.gov/11879257/</a>
221	<b>CYP3A4</b>	Simvastatin (po)	Diltiazem (po)	20 mg on day 15 (12 h after last Diltiazem dose)	120 mg BID for 14 days (28 doses)	10	19-35 years; 50% F	4.5	6.24	3.61	4.82	Mousa et al., 2000	<a href="https://pubmed.ncbi.nlm.nih.gov/10741630/">https://pubmed.ncbi.nlm.nih.gov/10741630/</a>
222	<b>CYP3A4</b>	Simvastatin (po)	Amiodarone (po)	40 mg on day 4	400 mg for 4 days	12	19-43 years; 42% F	1.5	1.59	1.56	1.54	Becquemenot et al., 2007	<a href="https://pubmed.ncbi.nlm.nih.gov/17301736/">https://pubmed.ncbi.nlm.nih.gov/17301736/</a>

223	<b>CYP3A4</b>	Simvastatin (po)	Erythromycin (po)	40 mg on Day 2	500 mg TID for 2 days	12	20-29 years; 33% F	7.11	10.15	3.46	6.21	Kantola et al., 1998	<a href="https://pubmed.ncbi.nlm.nih.gov/9728898/">https://pubmed.ncbi.nlm.nih.gov/9728898/</a>
224	<b>CYP3A4</b>	Simvastatin (po)	Verapamil (po)	40 mg on Day 2	80mg TID for 2 days	12	20-29 years; 33% F	7.12	9.08	2.56	4.65	Kantola et al., 1998	<a href="https://pubmed.ncbi.nlm.nih.gov/9728898/">https://pubmed.ncbi.nlm.nih.gov/9728898/</a>
225	<b>CYP3A4</b>	Simvastatin (po)	Ketoconazole (po)	40 mg on Day 6 (2hrs before Ketoconazole)	400 mg QD for 10 days	19	30-48 years; 53% F	3.65	8.37	7.43	12.55	Chung et al., 2006	<a href="https://pubmed.ncbi.nlm.nih.gov/16580903/">https://pubmed.ncbi.nlm.nih.gov/16580903/</a>
226	<b>CYP3A4</b>	Simvastatin (po)	Clarithromycin (po)	40 mg QD for 8 days	500 mg bid for 8 days	12	20-50 years; 50% F	11.16	19.38	7.14	9.95	Jacobson et al., 2000	<a href="https://pubmed.ncbi.nlm.nih.gov/15518608/">https://pubmed.ncbi.nlm.nih.gov/15518608/</a>
227	<b>CYP3A4</b>	Triazolam (po)	Diltiazem (po)	0.25 mg on day 2 (1h after 5th Diltiazem dose)	60 mg TID for 2 days (6 doses)	10	18-31 years; 70% F	1.46	2.2	1.86	3.38	Varhe et al., 1996	<a href="https://pubmed.ncbi.nlm.nih.gov/8612379/">https://pubmed.ncbi.nlm.nih.gov/8612379/</a>
228	<b>CYP3A4</b>	Triazolam (po)	Fluconazole (po)	0.25 mg on day 4 (1 hour after Fluconazole)	50 mg QD for 4 days at 1 pm	8	20-32 years; 63% F	1.25	1.52	1.47	1.63	Varhe et al., 1996	<a href="https://pubmed.ncbi.nlm.nih.gov/8904618/">https://pubmed.ncbi.nlm.nih.gov/8904618/</a>
229	<b>CYP3A4</b>	Triazolam (po)	Fluconazole (po)	0.25 mg on day 4 (1 hour after Fluconazole)	100 mg QD for 4 days at 1 pm	8	20-32 years; 63% F	1.43	2.01	1.4	2.05	Varhe et al., 1996	<a href="https://pubmed.ncbi.nlm.nih.gov/8904618/">https://pubmed.ncbi.nlm.nih.gov/8904618/</a>
230	<b>CYP3A4</b>	Triazolam (po)	Fluconazole (po)	0.25 mg on day 4 (1 hour after Fluconazole)	200 mg QD for 4 days at 1 pm	8	20-32 years; 63% F	1.65	2.92	2.33	4.42	Varhe et al., 1996	<a href="https://pubmed.ncbi.nlm.nih.gov/8904618/">https://pubmed.ncbi.nlm.nih.gov/8904618/</a>
231	<b>CYP3A4</b>	Triazolam (po)	Fluconazole (po)	0.25 mg on day 4 (1 hour after Fluconazole)	100 mg QD for 4 days at 2pm	12	19-31 years; 83% F	1.65	2.92	1.25	2.46	Varhe et al., 2005	<a href="https://pubmed.ncbi.nlm.nih.gov/8730978/">https://pubmed.ncbi.nlm.nih.gov/8730978/</a>
232	<b>CYP3A4</b>	Triazolam (po)	Ketoconazole (po)	0.25 mg on day 3 (1 h after Ketoconazole dose)	200 mg BID for 4 days (8 doses)	7	21-44 years; 0 F	2.42	12.41	2.08	13.72	Greenblatt et al., 1998	<a href="https://pubmed.ncbi.nlm.nih.gov/9757147/">https://pubmed.ncbi.nlm.nih.gov/9757147/</a>
233	<b>CYP3A4</b>	Triazolam (po)	Clarithromycin (po)	0.125 mg on day 2 (1h after 3rd Clarithromycin dose)	500 mg given at 8 am and 4 pm Day 1 and 8 am and 5 pm on Day 2, (4 doses)	12	21-39 years; 50% F	1.7	5.84	1.97	5.25	Greenblatt et al., 1999	<a href="https://pubmed.ncbi.nlm.nih.gov/9757151/">https://pubmed.ncbi.nlm.nih.gov/9757151/</a>
234	<b>CYP3A4</b>	Triazolam (po)	Cimetidine (po)	0.5 mg on Day 2	300 mg QID for 2 days	19	20-45 years; 50% F	1.36	1.55	1.39	1.32	Friedman et al., 1988	<a href="https://pubmed.ncbi.nlm.nih.gov/3360971/">https://pubmed.ncbi.nlm.nih.gov/3360971/</a>

235	<b>CYP3A4</b>	Triazolam (po)	Cimetidine (po)	0.5 mg QD at night for 7 days	200 mg TID with 400 mg at night for 9 days	8	22-25 years; 25% F	1.41	1.57	1.51	2.2	Pourbaix et al., 1985	<a href="https://pubmed.ncbi.nlm.nih.gov/2864320/">https://pubmed.ncbi.nlm.nih.gov/2864320/</a>
236	<b>CYP3A4</b>	Triazolam (po)	Cimetidine (po)	0.5 mg (1 hr after 3rd cimetidine dose)	300 mg QID (4 doses)	4	20-31 years; 0 F	1.3	1.42	1.35	1.55	Cox et al., 1986	<a href="https://pubmed.ncbi.nlm.nih.gov/3828486/">https://pubmed.ncbi.nlm.nih.gov/3828486/</a>
237	<b>CYP3A4</b>	Triazolam (po)	Erythromycin (po)	0.125 mg on day 2 at 3 pm	500 mg BID 2 days	12	21-39 years; 50% F	1.67	3.89	1.77	3.8	Greenblatt et al., 1998	<a href="https://pubmed.ncbi.nlm.nih.gov/9757151/">https://pubmed.ncbi.nlm.nih.gov/9757151/</a>
238	<b>CYP3A4</b>	Mirabegron (po)	Ketoconazole (po)	Mirabegron (OCAS tablets) 100mg SD on day 4	Ketoconazole 400mg once daily for 9 days	24	18-55 years; 50% F	1.31	1.84	1.45	1.81	Lee et al., 2013	<a href="https://pubmed.ncbi.nlm.nih.gov/23625188/">https://pubmed.ncbi.nlm.nih.gov/23625188/</a>
239	<b>CYP3A4</b>	Midazolam (po)	Cimetidine (po)	7.5mg SD	800 mg SD	8	20-26 years; 0 F	-	2	-	1.5	Martinez et al., 1999	<a href="https://pubmed.ncbi.nlm.nih.gov/10223772/">https://pubmed.ncbi.nlm.nih.gov/10223772/</a>
240	<b>CYP3A4</b>	Alprazolam (po)	Cimetidine (po)	1 mg on day 2	300 mg QID (14 doses)	9	24-48 years; 50% F	1.03	1.23	1.03	1.58	Abernethy et al., 1983	<a href="https://pubmed.ncbi.nlm.nih.gov/6137021/">https://pubmed.ncbi.nlm.nih.gov/6137021/</a>
241	<b>CYP3A4</b>	Nifedipine (po)	Cimetidine (po)	10 mg on day 2	400 mg TID for 4 doses	8	21-24 years; 0 F	1.43	1.7	1.84	1.84	Renwick et al., 1987	<a href="https://pubmed.ncbi.nlm.nih.gov/3609112/">https://pubmed.ncbi.nlm.nih.gov/3609112/</a>
242	<b>CYP3A4</b>	Carbamazepine (po)	Cimetidine (po)	600mg on day 3	300 mg QID for 9 days	8	24-35 years; 0 F	-	1.21	-	1.25	Dalton et al., 1985	<a href="https://pubmed.ncbi.nlm.nih.gov/3987645/">https://pubmed.ncbi.nlm.nih.gov/3987645/</a>
243	<b>CYP3A4</b>	Verapamil (po)	Cimetidine (po)	120mg on day 8	300 mg QID for 9 days	8	24-38 years; 0 F	1.25	1.35	1.13	1.37	Smith et al., 1984	<a href="https://pubmed.ncbi.nlm.nih.gov/6478741/">https://pubmed.ncbi.nlm.nih.gov/6478741/</a>
244	<b>CYP3A4</b>	Zolpidem (po)	Cimetidine (po)	16.08 mg on day 2	200 mg TID and 400mg at night on day 1; 200mg on day 2	6	20-50 years; 50% F	1.09	1.19	1.1	1.3	N/A	<a href="https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview_process&amp;varApplNo=019908">https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview_process&amp;varApplNo=019908</a>
245	<b>CYP3A4</b>	Alprazolam (po)	Fluvoxamine (po)	1 mg from day 7 to day 10, at 8:00, 13:00, 18:00, and 23:00	50 mg QD from day 1 to day 3 at 8:00 and 100 mg QD from day 4 to day 10 at 8:00	30	20-44 years; 0 F	1.06	1.08	1.86	1.96	Fleishaker et al., 2004	<a href="https://pubmed.ncbi.nlm.nih.gov/8005185/">https://pubmed.ncbi.nlm.nih.gov/8005185/</a>
246	<b>CYP3A4</b>	Midazolam (IV)	Fluvoxamine (po)	0.025 mg/kg SD IV on day 28	Fluvoxamine 150 mg QD oral for 28 days	20	27-48 years; 50% F	-	1.76	-	1.49	Chen et al., 2006	<a href="https://pubmed.ncbi.nlm.nih.gov/16842393/">https://pubmed.ncbi.nlm.nih.gov/16842393/</a>

