

Substrate-Inhibitor Matrix for CYP competitive and mechanism-based inhibition of CYP1A2, CYP2C8, CYP2C9, CYP2C19, and CYP3A4/5.

Substrate	Elimination Mechanisms included in the V19 model	Interaction parameters considered in V19	Inhibitor	FDA Index inhibitor	Mechanisms Considered in the V19 file
Midazolam	<b>CYP3A4</b> CYP3A5 UGT1A4 Renal	NA	Clarithromycin	<b>CYP3A4 (strong)</b> P-gp inhibition OATP1B1 inhibition OATP1B3 inhibition	<b>CYP3A4 competitive</b> <b>CYP3A4 MBI</b> OATP1B1 competitive OATP1B3 competitive P-gp Intestine and Liver competitive
Alfentanil	<b>CYP3A4</b> Renal HLM - not defined to an enzyme	NA	Fluconazole	CYP2C9 (moderate) CYP2C19 (strong) <b>CYP3A4 (moderate)</b>	CYP2C9 competitive CYP2C19 competitive <b>CYP3A4 competitive</b> CYP3A5 competitive UGT2B7 competitive
Alfentanil	<b>CYP3A4</b> Renal HLM - not defined to an enzyme	NA	Ketoconazole	<b>CYP3A4 (strong)</b> P-gp inhibition	CYP2C8 competitive CYP2C9 competitive <b>CYP3A4 competitive</b> <b>CYP3A5 competitive</b>
Alprazolam	<b>CYP3A4</b> <b>CYP3A5</b> Renal	NA	Ketoconazole	<b>CYP3A4 (strong)</b> P-gp inhibition	CYP2C8 competitive CYP2C9 competitive <b>CYP3A4 competitive</b> <b>CYP3A5 competitive</b>
Alprazolam	<b>CYP3A4</b> <b>CYP3A5</b> Renal	NA	Ritonavir	<b>CYP3A4 (strong)</b> CYP2C9 induction (weak) CYP2C19 induction (weak) CYP2B6 induction (weak) P-gp inhibition (in combination with saquinavir or lopinavir)	CYP2D6 competitive <b>CYP3A4 competitive</b> <b>CYP3A5 competitive</b> <b>CYP3A4 MBI</b> <b>CYP3A5 MBI</b> CYP2C9 induction <b>CYP3A4 induction</b> <b>CYP3A5 induction</b>

				OATP1B1/3 inhibition (in combination with atazanavir or lopinavir)	P-gp Intestine and Liver competitive
Alprazolam	<b>CYP3A4</b> CYP3A5 Renal	NA	Fluoxetine	CYP2C19 (strong) CYP2D6 (strong)	CYP2C19 competitive CYP2C19 MBI CYP2D6 competitive <b>CYP3A4 competitive</b> <b>CYP3A4 MBI</b> CYP2C19 competitive (norfluoxetine) CYP2C19 MBI (norfluoxetine) CYP2D6 competitive (norfluoxetine) <b>CYP3A4 competitive (norfluoxetine)</b> <b>CYP3A4 MBI (norfluoxetine)</b>
Alprazolam	<b>CYP3A4</b> CYP3A5 Renal	NA	Cimetidine	MATE1 inhibition MATE2-K inhibition OCT2 inhibition CYP1A2 (weak) CYP2D6 (weak) <b>CYP3A4 (weak)</b>	CYP2D6 competitive <b>CYP3A4 competitive</b> OCT1 Liver competitive MATEs Kidney competitive OCT2 Kidney competitive
Atazanavir	<b>CYP3A4</b> <b>CYP3A5</b> Renal HLM - not defined to an enzyme	CYP3A4 competitive CYP3A5 competitive CYP3A4 MBI CYP3A5 MBI UGT1A1 competitive	Ketoconazole	<b>CYP3A4 (strong)</b> P-gp inhibition	CYP2C8 competitive CYP2C9 competitive <b>CYP3A4 competitive</b> <b>CYP3A5 competitive</b>
Atazanavir	<b>CYP3A4</b> CYP3A5 Renal HLM - not defined to an enzyme	CYP3A4 competitive CYP3A5 competitive CYP3A4 MBI CYP3A5 MBI UGT1A1 competitive	Clarithromycin	<b>CYP3A4 (strong)</b> P-gp inhibition OATP1B1 inhibition OATP1B3 inhibition	<b>CYP3A4 competitive</b> <b>CYP3A4 MBI</b> OATP1B1 competitive OATP1B3 competitive P-gp Intestine and Liver competitive

Clarithromycin	<b>CYP3A4</b> Renal	CYP3A4 competitive CYP3A4 MBI OATP1B1 OATP1B3 P-gp Intestine and Liver competitive	Atazanavir	OATP1B1/3 inhibition (in combination with ritonavir)	<b>CYP3A4 competitive</b>  CYP3A5 competitive <b>CYP3A4 MBI</b> CYP3A5 MBI UGT1A1 competitive
Clarithromycin	<b>CYP3A4</b> Renal	CYP3A4 competitive CYP3A4 MBI  OATP1B1 competitive OATP1B3 competitive P-gp Intestine and Liver competitive	Ritonavir	P-gp inhibition (in combination with saquinavir or lopinavir) OATP1B1/3 inhibition (in combination with atazanavir or lopinavir) CYP2C9 induction (weak)  CYP2C19 induction (weak)  CYP2B6 induction (weak)  <b>CYP3A4 (strong)</b>	CYP2D6 competitive  <b>CYP3A4 competitive</b>  CYP3A5 competitive  <b>CYP3A4 MBI</b>  CYP3A5 MBI  CYP2C9 induction <b>CYP3A4 induction</b> CYP3A5 induction P-gp Intestine and Liver competitive
Midazolam	<b>CYP3A4</b> <b>CYP3A5</b> UGT1A4 Renal	NA	Fluconazole	CYP2C9 (moderate) CYP2C19 (strong) <b>CYP3A4 (moderate)</b>	CYP2C9 competitive CYP2C19 competitive <b>CYP3A4 competitive</b> <b>CYP3A5 competitive</b> UGT2B7 competitive
Midazolam	<b>CYP3A4</b> CYP3A5 UGT1A4 Renal	NA	Itraconazole	P-gp inhibition <b>CYP3A4 (strong)</b>	<b>CYP3A4 competitive</b> OATP1B3 competitive OATP1B1 competitive BCRP competitive CYP3A4 competitive (OH-metabolite) BCRP competitive (OH-metabolite) OATP1B3 competitive (OH-metabolite) OATP1B1 competitive (OH-metabolite)

					OATP2B1 competitive (OH-metabolite) NTCP competitive (OH-metabolite)
Midazolam	<b>CYP3A4</b>  <b>CYP3A5</b>  UGT1A4 Renal	NA	Ritonavir	P-gp inhibition (in combination with saquinavir or lopinavir) OATP1B1/3 inhibition (in combination with atazanavir or lopinavir) CYP2C9 induction (weak) CYP2C19 induction (weak) CYP2B6 induction (weak) <b>CYP3A4 (strong)</b>	CYP2D6 competitive  <b>CYP3A4 competitive</b>  <b>CYP3A5 competitive</b> <b>CYP3A4 MBI</b> <b>CYP3A5 MBI</b> CYP2C9 induction <b>CYP3A4 induction</b> <b>CYP3A5 induction</b> P-gp Intestine and Liver competitive
Midazolam	<b>CYP3A4</b>  <b>CYP3A5</b> UGT1A4 Renal	NA	Diltiazem	<b>CYP3A4 (moderate)</b>	<b>CYP3A4/5 competitive</b> <b>CYP3A4/5 MBI</b> <b>CYP3A4 competitive (metabolite)</b> <b>CYP3A4 MBI (metabolite)</b>
Midazolam	<b>CYP3A4</b>  <b>CYP3A5</b> UGT1A4 Renal	NA	Verapamil	P-gp inhibition <b>CYP3A4 (moderate)</b>	<b>CYP3A4 MBI (norverapamil)</b> <b>CYP3A5 MBI (norverapamil)</b> P-gp competitive (norverapamil) <b>CYP3A4 MBI</b> <b>CYP3A5 MBI</b> P-gp competitive
Midazolam	<b>CYP3A4</b>  <b>CYP3A5</b> UGT1A4 Renal	NA	Ketoconazole	<b>CYP3A4 (strong)</b> P-gp inhibition	CYP2C8 competitive CYP2C9 competitive <b>CYP3A4 competitive</b> <b>CYP3A5 competitive</b>
Midazolam	<b>CYP3A4</b> CYP3A5 UGT1A4 Renal	NA	Cimetidine	MATE1 inhibition MATE2-K inhibition OCT2 inhibition CYP1A2 (weak) CYP2D6 (weak)	CYP2D6 competitive <b>CYP3A4 competitive</b> OCT1 Liver competitive MATEs Kidney competitive OCT2 Kidney competitive

				<b>CYP3A4 (weak)</b>	
Midazolam	<b>CYP3A4</b> <b>CYP3A5</b> UGT1A4 Renal	NA	Erythromycin	<b>CYP3A4 moderate</b> P-gp inhibition	<b>CYP3A4 competitive</b> <b>CYP3A4/5 MBI</b>
Midazolam	<b>CYP3A4</b> <b>CYP3A5</b> UGT1A4 Renal	NA	Fluvoxamine	CYP1A2 (strong) CYP2C9 (weak) CYP2C19 (strong) CYP2D6 (weak) <b>CYP3A4 (moderate)</b>	CYP1A2 competitive CYP2C9 competitive CYP2C19 competitive CYP2D6 competitive <b>CYP3A4/5 competitive</b>
Phenytoin	<b>CYP2C9</b> CYP2C19 HLM - not defined to an enzyme Renal CL	CYP2B6 induction CYP2C9 induction CYP3A4 induction  CYP1A2 induction	Amiodarone	<b>CYP2C9 (moderate)</b> CYP2D6 (weak) P-gp inhibition	<b>CYP2C9 competitive</b> <b>CYP2C9 MBI</b> CYP2D6 competitive  CYP3A4 competitive CYP3A4 MBI CYP2C9 competitive (Mono-desethyl-amiodarone) CYP2D6 competitive (Mono-desethyl-amiodarone) CYP2D6 MBI (Mono-desethyl-amiodarone) CYP3A4 competitive (Mono-desethyl-amiodarone)
Nifedipine	<b>CYP3A4</b> CYP3A5 Renal	NA	Cimetidine	MATE1 inhibition MATE2-K inhibition OCT2 inhibition CYP1A2 (weak) CYP2D6 (weak) <b>CYP3A4 (weak)</b>	CYP2D6 competitive <b>CYP3A4 competitive</b> OCT1 Liver competitive MATEs Kidney competitive OCT2 Kidney competitive
Nifedipine	<b>CYP3A4</b> <b>CYP3A5</b> Renal	NA	Diltiazem	<b>CYP3A4 (moderate)</b>	<b>CYP3A4/5 competitive</b> <b>CYP3A4/5 MBI</b> <b>CYP3A4 competitive (metabolite)</b> <b>CYP3A4 MBI (metabolite)</b>

Quinidine	<b>CYP3A4</b>  CYP2C9  CYP2E1 Renal	CYP2D6 competitive CYP3A4 competitive P-gp competitive	Verapamil	P-gp inhibition  <b>CYP3A4 (moderate)</b>	<b>CYP3A4 MBI (norverapamil)</b>  <b>CYP3A5 MBI (norverapamil)</b>  P-gp competitive (norverapamil) <b>CYP3A4 MBI</b> <b>CYP3A5 MBI</b> P-gp competitive
Quinidine	<b>CYP3A4</b>  CYP2C9  CYP2E1 Renal	CYP2D6 competitive CYP3A4 competitive P-gp competitive	Diltiazem	<b>CYP3A4 (moderate)</b>	<b>CYP3A4/5 competitive</b>  <b>CYP3A4/5 MBI</b>  <b>CYP3A4 competitive (metabolite)</b> <b>CYP3A4 MBI (metabolite)</b>
Quinidine	<b>CYP3A4</b>  CYP2C9  CYP2E1 Renal	CYP2D6 competitive CYP3A4 competitive P-gp competitive	Cimetidine	MATE1 inhibition  MATE2-K inhibition  OCT2 inhibition CYP1A2 (weak) CYP2D6 (weak) <b>CYP3A4 (weak)</b>	CYP2D6 competitive  <b>CYP3A4 competitive</b>  OCT1 Liver competitive MATEs Kidney competitive OCT2 Kidney competitive
Quinidine	<b>CYP3A4</b>  CYP2C9  CYP2E1 Renal	CYP2D6 competitive CYP3A4 competitive P-gp competitive	Itraconazole	<b>P-gp inhibition</b>  CYP3A4 (strong)	<b>CYP3A4 competitive</b>  OATP1B3 competitive  OATP1B1 competitive BCRP competitive <b>CYP3A4 competitive (OH-metabolite)</b> BCRP competitive (OH-metabolite) OATP1B3 competitive (OH-metabolite) OATP1B1 competitive (OH-metabolite) OATP2B1 competitive (OH-metabolite) NTCP competitive (OH-metabolite)
Quinidine	<b>CYP3A4</b>	CYP2D6 competitive	Erythromycin	<b>CYP3A4 moderate</b>	<b>CYP3A4 competitive</b>

	CYP2C9 CYP2E1 Renal	CYP3A4 competitive P-gp competitive		P-gp inhibition	<b>CYP3A4/5 MBI</b>
Quinidine	<b>CYP3A4</b> <b>CYP2C9</b> CYP2E1 Renal	CYP2D6 competitive CYP3A4 competitive P-gp competitive	Fluvoxamine	CYP1A2 (strong) <b>CYP2C9 (weak)</b> CYP2C19 (strong) CYP2D6 (weak) <b>CYP3A4 (moderate)</b>	CYP1A2 competitive <b>CYP2C9 competitive</b> CYP2C19 competitive CYP2D6 competitive <b>CYP3A4/5 competitive</b>
Repaglinide	CYP2C8 <b>CYP3A4</b> Renal OATP1B1	NA	Itraconazole	P-gp inhibition <b>CYP3A4 (strong)</b>	<b>CYP3A4 competitive</b> OATP1B3 competitive OATP1B1 competitive BCRP competitive CYP3A4 competitive (OH-metabolite) BCRP competitive (OH-metabolite) OATP1B3 competitive (OH-metabolite) OATP1B1 competitive (OH-metabolite) OATP2B1 competitive (OH-metabolite) NTCP competitive (OH-metabolite)
Repaglinide	CYP2C8 <b>CYP3A4</b> Renal OATP1B1	NA	Cyclosporine	P-gp inhibition BCRP inhibition OATP1B1 inhibition OATP1B3 inhibition <b>CYP3A4 (moderate)</b>	<b>CYP3A4 competitive</b> P-gp competitive BCRP competitive NTCP competitive OATP1B1 competitive OATP1B3 competitive OATP2B1 competitive
Repaglinide	CYP2C8 <b>CYP3A4</b> Renal OATP1B1	NA	Clarithromycin	<b>CYP3A4 (strong)</b> P-gp inhibition OATP1B1 inhibition OATP1B3 inhibition	<b>CYP3A4 competitive</b> <b>CYP3A4 MBI</b> OATP1B1 competitive OATP1B3 competitive P-gp Intestine and Liver competitive

Sildenafil	CYP2C9 <b>CYP3A4</b> Renal CL	NA	Clarithromycin	<b>CYP3A4 (strong)</b> P-gp inhibition OATP1B1 inhibition OATP1B3 inhibition	<b>CYP3A4 competitive</b> <b>CYP3A4 MBI</b> OATP1B1 OATP1B3 P-gp Intestine and Liver competitive
Sildenafil	CYP2C9 <b>CYP3A4</b> Renal CL	NA	Erythromycin	<b>CYP3A4 moderate</b> P-gp inhibition	<b>CYP3A4 competitive</b> <b>CYP3A4/5 MBI</b>
Sildenafil	<b>CYP2C9</b>  <b>CYP3A4</b>  Renal CL	NA	Ritonavir	P-gp inhibition (in combination with saquinavir or lopinavir) OATP1B1/3 (in combination with atazanavir or lopinavir) <b>CYP2C9 induction (weak)</b> CYP2C19 induction (weak) CYP2B6 induction (weak) <b>CYP3A4 (strong)</b>	CYP2D6 competitive  <b>CYP3A4 competitive</b>  CYP3A5 competitive CYP3A4 MBI CYP3A5 MBI <b>CYP2C9 induction</b> <b>CYP3A4 induction</b> CYP3A5 induction P-gp Intestine and Liver competitive
Sildenafil	CYP2C9 <b>CYP3A4</b> Renal CL	NA	Cimetidine	MATE1 inhibition MATE2-K inhibition OCT2 inhibition CYP1A2 (weak) CYP2D6 (weak) <b>CYP3A4 (weak)</b>	CYP2D6 competitive <b>CYP3A4 competitive</b> OCT1 Liver competitive MATEs Kidney competitive OCT2 Kidney competitive
Simvastatin	<b>CYP3A4</b> HLM - not defined to an enzyme HIMMs - not defined to an enzyme	NA	Diltiazem	<b>CYP3A4 (moderate)</b>	<b>CYP3A4/5 competitive</b> <b>CYP3A4/5 MBI</b>  <b>CYP3A4 competitive (metabolite)</b>  <b>CYP3A4 MBI (metabolite)</b>
Simvastatin	<b>CYP3A4</b> HLM - not defined to an enzyme	NA	Erythromycin	<b>CYP3A4 moderate</b> P-gp inhibition	<b>CYP3A4 competitive</b> <b>CYP3A4/5 MBI</b>



	HIMMs - not defined to an enzyme				
Simvastatin	<b>CYP3A4</b> HLM - not defined to an enzyme HIMMs - not defined to an enzyme	NA	Verapamil	<b>P-gp inhibition</b> CYP3A4 (moderate)	<b>CYP3A4 MBI (norverapamil)</b> CYP3A5 MBI (norverapamil) P-gp competitive (norverapamil) <b>CYP3A4 MBI</b> CYP3A5 MBI P-gp competitive
Simvastatin	<b>CYP3A4</b> HLM - not defined to an enzyme HIMMs - not defined to an enzyme	NA	Ketoconazole	<b>CYP3A4 (strong)</b> P-gp inhibition	CYP2C8 competitive CYP2C9 competitive  <b>CYP3A4 competitive</b>  CYP3A5 competitive
Simvastatin	<b>CYP3A4</b> HLM - not defined to an enzyme HIMMs - not defined to an enzyme	NA	Clarithromycin	<b>CYP3A4 (strong)</b> P-gp inhibition OATP1B1 inhibition OATP1B3 inhibition	<b>CYP3A4 competitive</b> <b>CYP3A4 MBI</b> OATP1B1 competitive OATP1B3 competitive P-gp Intestine and Liver competitive
Triazolam	<b>CYP3A4</b> <b>CYP3A5</b> Renal	NA	Diltiazem	<b>CYP3A4 (moderate)</b>	<b>CYP3A4/5 competitive</b> <b>CYP3A4/5 MBI</b> <b>CYP3A4 competitive (metabolite)</b> <b>CYP3A4 MBI (metabolite)</b>
Triazolam	<b>CYP3A4</b> <b>CYP3A5</b> Renal	NA	Fluconazole	CYP2C9 (moderate) CYP2C19 (strong) <b>CYP3A4 (moderate)</b>	CYP2C9 competitive CYP2C19 competitive <b>CYP3A4 competitive</b> <b>CYP3A5 competitive</b> UGT2B7 competitive
Triazolam	<b>CYP3A4</b> <b>CYP3A5</b> Renal	NA	Ketoconazole	<b>CYP3A4 (strong)</b> P-gp inhibition	CYP2C8 competitive CYP2C9 competitive <b>CYP3A4 competitive</b> <b>CYP3A5 competitive</b>
Triazolam	<b>CYP3A4</b>	NA	Clarithromycin	<b>CYP3A4 (strong)</b>	<b>CYP3A4 competitive</b>

	CYP3A5 Renal			P-gp inhibition OATP1B1 inhibition OATP1B3 inhibition	<b>CYP3A4 MBI</b> OATP1B1 competitive OATP1B3 competitive P-gp Intestine and Liver competitive
Triazolam	<b>CYP3A4</b> CYP3A5 Renal	NA	Cimetidine	MATE1 inhibition MATE2-K inhibition OCT2 inhibition CYP1A2 (weak) CYP2D6 (weak) <b>CYP3A4 (weak)</b>	CYP2D6 competitive <b>CYP3A4 competitive</b> OCT1 Liver competitive MATEs Kidney competitive OCT2 Kidney competitive
Triazolam	<b>CYP3A4</b> <b>CYP3A5</b> Renal	NA	Erythromycin	<b>CYP3A4 moderate</b> P-gp inhibition	<b>CYP3A4 competitive</b> <b>CYP3A4/5 MBI</b>
Triazolam	<b>CYP3A4</b> CYP3A5 Renal	NA	Itraconazole	P-gp inhibition <b>CYP3A4 (strong)</b>	<b>CYP3A4 competitive</b> OATP1B3 competitive OATP1B1 competitive BCRP competitive <b>CYP3A4 competitive (OH-metabolite)</b> BCRP competitive (OH-metabolite) OATP1B3 competitive (OH-metabolite) OATP1B1 competitive (OH-metabolite) OATP2B1 competitive (OH-metabolite) NTCP competitive (OH-metabolite)
Zolpidem	CYP1A2 CYP2C9 CYP2C19 CYP2D6 <b>CYP3A4</b>	NA	Itraconazole	P-gp inhibition <b>CYP3A4 (strong)</b>	<b>CYP3A4 competitive</b> OATP1B3 competitive OATP1B1 competitive BCRP competitive <b>CYP3A4 competitive (OH-metabolite)</b> BCRP competitive (OH-metabolite) OATP1B3 competitive (OH-metabolite) OATP1B1 competitive (OH-metabolite) OATP2B1 competitive (OH-metabolite)

					NTCP competitive (OH-metabolite)
S-Warfarin	Renal <b>CYP2C9 (allelics)</b>	NA	Fluconazole	<b>CYP2C9 (moderate)</b> CYP2C19 (strong) CYP3A4 (moderate)	<b>CYP2C9 competitive</b> CYP2C19 competitive CYP3A4 competitive CYP3A5 competitive UGT2B7 competitive
Tolbutamide	<b>CYP2C9</b> <b>CYP2C19</b> Renal	NA	Fluconazole	<b>CYP2C9 (moderate)</b> <b>CYP2C19 (strong)</b> CYP3A4 (moderate)	<b>CYP2C9 competitive</b> <b>CYP2C19 competitive</b> CYP3A4 competitive CYP3A5 competitive UGT2B7 competitive
Phenytoin	<b>CYP2C9</b> <b>CYP2C19</b> HLM - not defined to an enzyme Renal CL	CYP2B6 induction CYP2C9 induction CYP3A4 induction  CYP1A2 induction	Fluconazole	<b>CYP2C9 (moderate)</b> <b>CYP2C19 (strong)</b> CYP3A4 (moderate)	<b>CYP2C9 competitive</b> <b>CYP2C19 competitive</b> CYP3A4 competitive  CYP3A5 competitive UGT2B7 competitive
Celecoxib	<b>CYP2C9 (allelics)</b> <b>CYP3A4</b> HLM - not defined to an enzyme Renal CL	NA	Fluconazole	<b>CYP2C9 (moderate)</b> CYP2C19 (strong) <b>CYP3A4 (moderate)</b>	<b>CYP2C9 competitive</b> CYP2C19 competitive <b>CYP3A4 competitive</b>  CYP3A5 competitive UGT2B7 competitive
Tolbutamide	<b>CYP2C9</b> <b>CYP2C19</b> Renal	NA	Fluvoxamine	CYP1A2 (strong) <b>CYP2C9 (weak)</b> <b>CYP2C19 (strong)</b> CYP2D6 (weak) CYP3A4 (moderate)	CYP1A2 competitive <b>CYP2C9 competitive</b> <b>CYP2C19 competitive</b> CYP2D6 competitive CYP3A4/5 competitive
Phenytoin	<b>CYP2C9</b> <b>CYP2C19</b> HLM - not defined to an enzyme Renal CL	CYP2B6 induction CYP2C9 induction CYP3A4 induction  CYP1A2 induction	Sulphaphenazole	NA - in vivo	<b>CYP2C9 competitive</b> <b>CYP2C19 competitive</b>

Tolbutamide	<b>CYP2C9</b> <b>CYP2C19</b> Renal	NA	Sulphaphenazole	NA - in vivo	<b>CYP2C9 competitive</b> <b>CYP2C19 competitive</b>
Atomoxetine	<b>CYP2D6</b> <b>CYP2C19</b> HLM - not defined to an enzyme Renal CI	NA	Fluvoxamine	CYP1A2 (strong) CYP2C9 (weak) <b>CYP2C19 (strong)</b> <b>CYP2D6 (weak)</b> CYP3A4 (moderate)	CYP1A2 competitive CYP2C9 competitive <b>CYP2C19 competitive</b> <b>CYP2D6 competitive</b> CYP3A4/5 competitive
Atomoxetine	<b>CYP2D6</b> CYP2C19 HLM - not defined to an enzyme Renal CI	NA	Paroxetine	<b>CYP2D6 (strong)</b>	<b>CYP2D6 competitive</b> CYP3A4 competitive <b>CYP2D6 (MBI)</b> CYP3A4 (MBI)
Desipramine	Renal CL CYP2D6 cytosol- not defined to an enzyme	NA	Paroxetine	CYP2D6 (strong)	CYP2D6 competitive CYP3A4 competitive CYP2D6 (MBI) CYP3A4 (MBI)
Desipramine	Renal CL <b>CYP2D6</b> cytosol- not defined to an enzyme	NA	Fluoxetine	CYP2C19 (strong) <b>CYP2D6 (strong)</b>	CYP2C19 competitive CYP2C19 MBI <b>CYP2D6 competitive</b>  CYP3A4 competitive CYP3A4 MBI CYP2C19 competitive (norfluoxetine) CYP2C19 MBI (norfluoxetine) <b>CYP2D6 competitive (norfluoxetine)</b> CYP3A4 competitive (norfluoxetine) CYP3A4 MBI (norfluoxetine)
Desipramine	Renal CL <b>CYP2D6</b> cytosol- not defined to an enzyme	NA	Bupropion	<b>CYP2D6 (strong)</b>	<b>CYP2D6 competitive</b> <b>CYP2D6 competitive (metabolite)</b>

Desipramine	Renal CL  <b>CYP2D6</b>  cytosol- not defined to an enzyme	NA	Ritonavir	P-gp inhibition (in combination with saquinavir or lopinavir) OATP1B1/3 inhibition (in combination with atazanavir or lopinavir) CYP2C9 induction (weak)  CYP2C19 induction (weak) CYP2B6 induction (weak) CYP3A4 (strong)	<b>CYP2D6 competitive</b>  CYP3A4 competitive  CYP3A5 competitive  CYP3A4 MBI CYP3A5 MBI CYP2C9 induction CYP3A4 induction CYP3A5 induction P-gp Intestine and Liver competitive
Dextromethorphan	CYP2B6 CYP2C9 CYP2C18 CYP2C19 <b>CYP2D6</b> <b>CYP3A4</b> Renal Cl	NA	Quinidine	<b>CYP2D6 (strong)</b> P-gp inhibition	<b>CYP2D6 competitive</b> <b>CYP3A4 competitive</b> P-gp competitive
Dextromethorphan	CYP2B6 CYP2C9 CYP2C18 <b>CYP2C19</b> <b>CYP2D6</b> <b>CYP3A4</b> Renal Cl	NA	Fluoxetine	<b>CYP2C19 (strong)</b> <b>CYP2D6 (strong)</b>	<b>CYP2C19 competitive</b> <b>CYP2C19 MBI</b> <b>CYP2D6 competitive</b> <b>CYP3A4 competitive</b> <b>CYP3A4 MBI</b> <b>CYP2C19 competitive (norfluoxetine)</b> <b>CYP2C19 MBI (norfluoxetine)</b> <b>CYP2D6 competitive (norfluoxetine)</b> <b>CYP3A4 competitive (norfluoxetine)</b> <b>CYP3A4 MBI (norfluoxetine)</b>
Metoprolol	<b>CYP2D6</b> <b>CYP3A4</b> Renal Cl	NA	Paroxetine	<b>CYP2D6 (strong)</b>	<b>CYP2D6 competitive</b> <b>CYP3A4 competitive</b> <b>CYP2D6 (MBI)</b>

					<b>CYP3A4 (MBI)</b>
Metoprolol	<b>CYP2D6</b> <b>CYP3A4</b> Renal Cl	NA	Quinidine	<b>CYP2D6 (strong)</b> P-gp inhibition	<b>CYP2D6 competitive</b> <b>CYP3A4 competitive</b> P-gp competitive
Tolterodine	<b>CYP2D6</b> <b>CYP3A4</b> Renal Cl	NA	Fluoxetine	CYP2C19 (strong) <b>CYP2D6 (strong)</b>	CYP2C19 competitive CYP2C19 MBI <b>CYP2D6 competitive</b> <b>CYP3A4 competitive</b> <b>CYP3A4 MBI</b> CYP2C19 competitive (norfluoxetine) CYP2C19 MBI (norfluoxetine) <b>CYP2D6 competitive (norfluoxetine)</b> <b>CYP3A4 competitive (norfluoxetine)</b> <b>CYP3A4 MBI (norfluoxetine)</b>
Repaglinide	<b>CYP2C8</b> CYP3A4 Renal <b>OATP1B1</b>	NA	Trimethoprim	<b>CYP2C8 (weak)</b>	<b>CYP2C8 competitive</b> OCT2 Kidney competitive MATEs Kidney competitive OCT1 Liver competitive
Repaglinide	<b>CYP2C8</b> CYP3A4 Renal <b>OATP1B1</b>	NA	Gemfibrozil	<b>OATP1B1 inhibition</b> OATP1B3 inhibition <b>CYP2C8 (strong)</b>	<b>CYP2C8 competitive</b> CYP2C9 competitive OAT3 Kidney competitive <b>OATP1B1 competitive</b> OATP1B3 competitive OAT3 Kidney competitive (metabolite) <b>OATP1B1 competitive (metabolite)</b> <b>CYP2C8 competitive (metabolite)</b> <b>CYP2C8 MBI (metabolite)</b>
Rosiglitazone	<b>CYP2C8</b> CYP2C9 HLM - not defined to an enzyme	NA	Trimethoprim	<b>CYP2C8 (weak)</b>	<b>CYP2C8 competitive</b> OCT2 Kidney competitive MATEs OCT1 Liver competitive

Rosiglitazone	<b>CYP2C8</b> <b>CYP2C9</b> HLM - not defined to an enzyme	NA	Gemfibrozil	OATP1B1 inhibition OATP1B3 inhibition <b>CYP2C8 (strong)</b>	<b>CYP2C8 competitive</b> <b>CYP2C9 competitive</b> OAT3 Kidney competitive  OATP1B1 competitive OATP1B3 competitive OAT3 Kidney competitive (metabolite) OATP1B1 competitive (metabolite) <b>CYP2C8 competitive (metabolite)</b> <b>CYP2C8 MBI (metabolite)</b>
Caffeine	<b>CYP1A2</b> CYP2E1 Renal CL	NA	Ciprofloxacin	<b>CYP1A2 (strong)</b> CYP3A4 (moderate)	<b>CYP1A2 competitive</b> CYP3A4 competitive
Caffeine	<b>CYP1A2</b> CYP2E1 Renal CL	NA	Fluvoxamine	<b>CYP1A2 (strong)</b> CYP2C9 (weak) CYP2C19 (strong) CYP2D6 (weak) CYP3A4 (moderate)	<b>CYP1A2 competitive</b> CYP2C9 competitive CYP2C19 competitive CYP2D6 competitive CYP3A4/5 competitive
Theophylline	<b>CYP1A2</b> CYP2D6 <b>CYP3A4</b> CYP2E1 Renal Cl	NA	Ciprofloxacin	<b>CYP1A2 (strong)</b> <b>CYP3A4 (moderate)</b>	<b>CYP1A2 competitive</b> <b>CYP3A4 competitive</b>
Theophylline	<b>CYP1A2</b> <b>CYP2D6</b> <b>CYP3A4</b> CYP2E1 Renal Cl	NA	Fluvoxamine	<b>CYP1A2 (strong)</b> CYP2C9 (weak) CYP2C19 (strong) <b>CYP2D6 (weak)</b> <b>CYP3A4 (moderate)</b>	<b>CYP1A2 competitive</b> CYP2C9 competitive CYP2C19 competitive <b>CYP2D6 competitive</b> <b>CYP3A4/5 competitive</b>
S-Mephenytoin	<b>CYP2C9</b> <b>CYP2C19</b> Renal Cl	NA	Fluvoxamine	CYP1A2 (strong) <b>CYP2C9 (weak)</b> <b>CYP2C19 (strong)</b> CYP2D6 (weak)	CYP1A2 competitive <b>CYP2C9 competitive</b> <b>CYP2C19 competitive</b> CYP2D6 competitive

				CYP3A4 (moderate)	CYP3A4/5 competitive
Omeprazole	<b>CYP2C19</b> <b>CYP3A4</b>	CYP2C19 MBI CYP1A2 induction	Fluvoxamine	CYP1A2 (strong) CYP2C9 (weak) <b>CYP2C19 (strong)</b> CYP2D6 (weak) <b>CYP3A4 (moderate)</b>	CYP1A2 competitive CYP2C9 competitive <b>CYP2C19 competitive</b> CYP2D6 competitive <b>CYP3A4/5 competitive</b>
Omeprazole	<b>CYP2C19</b> <b>CYP3A4</b>	CYP2C19 MBI CYP1A2 induction	Fluoxetine	<b>CYP2C19 (strong)</b> CYP2D6 (strong)	<b>CYP2C19 competitive</b> <b>CYP2C19 MBI</b> CYP2D6 competitive <b>CYP3A4 competitive</b> <b>CYP3A4 MBI</b> <b>CYP2C19 competitive (norfluoxetine)</b> <b>CYP2C19 MBI (norfluoxetine)</b> CYP2D6 competitive (norfluoxetine) <b>CYP3A4 competitive (norfluoxetine)</b> <b>CYP3A4 MBI (norfluoxetine)</b>
Imipramine	CYP1A2 <b>CYP2C19</b> <b>CYP2D6</b> <b>CYP3A4</b> HLM - not defined to an enzyme Renal CI	NA	Fluoxetine	<b>CYP2C19 (strong)</b> <b>CYP2D6 (strong)</b>	<b>CYP2C19 competitive</b> <b>CYP2C19 MBI</b> <b>CYP2D6 competitive</b> <b>CYP3A4 competitive</b> <b>CYP3A4 MBI</b>  <b>CYP2C19 competitive (norfluoxetine)</b> <b>CYP2C19 MBI (norfluoxetine)</b> <b>CYP2D6 competitive (norfluoxetine)</b> <b>CYP3A4 competitive (norfluoxetine)</b> <b>CYP3A4 MBI (norfluoxetine)</b>
Omeprazole	<b>CYP2C19</b> CYP3A4	CYP2C19 MBI CYP1A2 induction	Ticlopidine	CYP2B6 (weak) <b>CYP2C19 (strong)</b>	CYP2B6 (MBI) <b>CYP2C19 (MBI)</b>
Tizanidine	<b>CYP1A2</b> Renal CI	NA	Fluvoxamine	<b>CYP1A2 (strong)</b> CYP2C9 (weak) CYP2C19 (strong)	<b>CYP1A2 competitive</b> CYP2C9 competitive CYP2C19 competitive



				CYP2D6 (weak) CYP3A4 (moderate)	CYP2D6 competitive CYP3A4/5 competitive
Tizanidine	<b>CYP1A2</b> Renal CL	NA	Ciprofloxacin	<b>CYP1A2 (strong)</b> CYP3A4 (moderate)	<b>CYP1A2 competitive</b> CYP3A4 competitive
Aprepitant	<b>CYP3A4</b> HLM - not defined to an enzyme Additional systemic clearance	CYP3A4 induction CYP3A4 inhibition  CYP3A4 MBI  CYP2C9 induction	Ketoconazole	<b>CYP3A4 (strong)</b> P-gp inhibition	CYP2C8 competitive CYP2C9 competitive  <b>CYP3A4 competitive</b>  CYP3A5 competitive
Dexamethasone	<b>CYP3A4</b> HLM - not defined to an enzyme Renal CL	CYP3A4 induction	Itraconazole	P-gp inhibition <b>CYP3A4 (strong)</b>	<b>CYP3A4 competitive</b> OATP1B3 competitive  OATP1B1 competitive BCRP competitive CYP3A4 competitive (OH-metabolite) BCRP competitive (OH-metabolite) OATP1B3 competitive (OH-metabolite) OATP1B1 competitive (OH-metabolite) OATP2B1 competitive (OH-metabolite) NTCP competitive (OH-metabolite)
Dexamethasone	<b>CYP3A4</b> HLM - not defined to an enzyme  Renal CL	CYP3A4 induction	Aprepitant	<b>CYP3A4 (moderate)</b> CYP2C9 induction (weak)	<b>CYP3A4 competitive</b> <b>CYP3A4 MBI</b> CYP2C9 induction <b>CYP3A4 induction</b>
Ibrutinib	<b>CYP3A4</b> HLM - not defined to an enzyme Renal CL	NA	Ketoconazole	<b>CYP3A4 (strong)</b> P-gp inhibition	CYP2C8 competitive CYP2C9 competitive  <b>CYP3A4 competitive</b> CYP3A5 competitive
Ibrutinib	<b>CYP3A4</b> HLM - not defined to an enzyme Renal CL	NA	Itraconazole	<b>CYP3A4 (strong)</b> P-gp inhibition	<b>CYP3A4 competitive</b> OATP1B3 competitive  OATP1B1 competitive

					BCRP competitive <b>CYP3A4 competitive (OH-metabolite)</b> BCRP competitive (OH-metabolite) OATP1B3 competitive (OH-metabolite) OATP1B1 competitive (OH-metabolite) OATP2B1 competitive (OH-metabolite) NTCP competitive (OH-metabolite)
Midazolam	<b>CYP3A4</b> CYP3A5 UGT1A4 Renal CL	NA	Aprepitant	<b>CYP3A4 (moderate)</b> CYP2C9 induction (weak)	<b>CYP3A4 competitive</b> <b>CYP3A4 MBI</b> <b>CYP3A4 induction</b> CYP2C9 induction
Rifabutin	<b>CYP3A4</b> CYP2J2 Renal CL	CYP2J2 induction CYP3A4 induction CYP3A5 induction	Fluconazole	CYP2C9 (moderate) CYP2C19 (strong) <b>CYP3A4 (moderate)</b>	CYP2C9 competitive CYP2C19 competitive <b>CYP3A4 competitive</b> CYP3A5 competitive UGT2B7 competitive
Rifabutin	<b>CYP3A4</b>  CYP2J2  Renal CL	CYP2J2 induction  CYP3A4 induction  CYP3A5 induction	Ritonavir	P-gp inhibition (in combination with saquinavir or lopinavir) OATP1B1/3 (in combination with atazanavir or lopinavir) CYP2C9 induction (weak) CYP2C19 induction (weak) CYP2B6 induction (weak) <b>CYP3A4 (strong)</b>	CYP2D6 competitive  <b>CYP3A4 competitive</b>  CYP3A5 competitive <b>CYP3A4 MBI</b> CYP3A5 MBI CYP2C9 induction <b>CYP3A4 induction</b> CYP3A5 induction P-gp Intestine and Liver competitive
Rifabutin	<b>CYP3A4</b> CYP2J2 Renal CL	CYP2J2 induction CYP3A4 induction CYP3A5 induction	Clarithromycin	<b>CYP3A4 (strong)</b> P-gp inhibition OATP1B1 OATP1B3	<b>CYP3A4 competitive</b> <b>CYP3A4 MBI</b> OATP1B1 OATP1B3 P-gp Intestine and Liver competitive
Simvastatin	<b>CYP3A4</b>	NA	Amiodarone	CYP2C9 (moderate)	CYP2C9 competitive

	HLM - not defined to an enzyme HIMMs - not defined to an enzyme			CYP2D6 (weak)  P-gp inhibition	CYP2C9 MBI  CYP2D6 competitive  <b>CYP3A4 competitive</b> <b>CYP3A4 MBI</b> CYP2C9 competitive (Mono-desethyl-amiodarone) CYP2D6 competitive (Mono-desethyl-amiodarone) CYP2D6 MBI (Mono-desethyl-amiodarone) <b>CYP3A4 competitive (Mono-desethyl-amiodarone)</b>
Flurbiprofen	<b>CYP2C9 (allelics)</b> <b>UGT2B7</b>	NA	Fluconazole	<b>CYP2C9 (moderate)</b> CYP2C19 (strong) CYP3A4 (moderate)	<b>CYP2C9 competitive</b> CYP2C19 competitive CYP3A4 competitive CYP3A5 competitive <b>UGT2B7 competitive</b>
S-Warfarin	Renal <b>CYP2C9 (allelics)</b>	NA	Amiodarone	<b>CYP2C9 (moderate)</b> CYP2D6 (weak) P-gp inhibition	<b>CYP2C9 competitive</b> <b>CYP2C9 MBI</b> CYP2D6 competitive CYP3A4 competitive CYP3A4 MBI <b>CYP2C9 competitive (metabolite)</b> CYP2D6 competitive (metabolite) CYP2D6 MBI (metabolite) CYP3A4 competitive (metabolite)
Desipramine	<b>CYP2D6</b> Renal CL cytosol- not defined to an enzyme	NA	Cinacalcet	<b>CYP2D6 (moderate)</b>	<b>CYP2D6 competitive</b>
Nebivolol	<b>CYP3A4</b> <b>CYP2D6</b> HLM - not defined to an enzyme	NA	Paroxetine	<b>CYP2D6 (strong)</b>	<b>CYP2D6 competitive</b> CYP3A4 competitive <b>CYP2D6 (MBI)</b>

					<b>CYP3A4 (MBI)</b>
Nebivolol	CYP3A4 <b>CYP2D6</b> HLM - not defined to an enzyme	NA	Bupropion	<b>CYP2D6 (strong)</b>	<b>CYP2D6 competitive</b> <b>CYP2D6 competitive (metabolite)</b>
Nebivolol	<b>CYP3A4</b> <b>CYP2D6</b> HLM - not defined to an enzyme	NA	Fluvoxamine	CYP1A2 (strong) CYP2C9 (weak) CYP2C19 (strong)  <b>CYP2D6 (weak)</b> <b>CYP3A4 (moderate)</b>	CYP1A2 competitive CYP2C9 competitive CYP2C19 competitive  <b>CYP2D6 competitive</b> <b>CYP3A4/5 competitive</b>
Nebivolol	<b>CYP3A4</b> <b>CYP2D6</b> HLM - not defined to an enzyme	NA	Fluoxetine	CYP2C19 (strong) <b>CYP2D6 (strong)</b>	CYP2C19 competitive CYP2C19 MBI <b>CYP2D6 competitive</b>  <b>CYP3A4 competitive</b> <b>CYP3A4 MBI</b> CYP2C19 competitive (norfluoxetine) CYP2C19 MBI (norfluoxetine) <b>CYP2D6 competitive (norfluoxetine)</b> <b>CYP3A4 competitive (norfluoxetine)</b> <b>CYP3A4 MBI (norfluoxetine)</b>