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	СҮРЗА4	NA	Clarithromycin	CYP3A4 (strong)	CYP3A4 competitive
	CYP3A5			P-gp inhibition	СҮРЗА4 МВІ
	UGT1A4			OATP1B1 inhibition	OATP1B1 competitive
	Renal			OATP1B3 inhibition	OATP1B3 competitive
					P-gp Intestine and Liver competitive
Alfentanil	СҮРЗА4	NA	Fluconazole	CYP2C9 (moderate)	CYP2C9 competitive
	Renal			CYP2C19 (strong)	CYP2C19 competitive
	HLM - not defined to an			CYP3A4 (moderate)	CYP3A4 competitive
	enzyme				CYP3A5 competitive
					UGT2B7 competitive
Alfentanil	СҮРЗА4	NA	Ketoconazole	CYP3A4 (strong)	CYP2C8 competitive
	Renal			P-gp inhibition	CYP2C9 competitive
	HLM - not defined to an				CYP3A4 competitive
	enzyme				CYP3A5 competitive
Alprazolam	СҮРЗА4		Ketoconazole	CYP3A4 (strong)	CYP2C8 competitive
	СҮРЗА5	NA		P-gp inhibition	CYP2C9 competitive
	Renal				CYP3A4 competitive
					CYP3A5 competitive
Alprazolam	СҮРЗА4	NA	Ritonavir	CYP3A4 (strong)	CYP2D6 competitive
	СҮРЗА5			CYP2C9 induction (weak)	CYP3A4 competitive
	Renal			CYP2C19 induction (weak)	CYP3A5 competitive
				CYP2B6 induction (weak)	СҮРЗА4 МВІ
				P-gp inhibition (in combination	СҮРЗА5 МВІ
				with saquinavir or lopinavir)	CYP2C9 induction
					CYP3A4 induction
					CYP3A5 induction

				OATP1B1/3 inhibition (in combination with atazanavir or lopinavir)	P-gp Intestine and Liver competitive
Alprazolam	СҮРЗА4	NA	Fluoxetine	CYP2C19 (strong)	CYP2C19 competitive
	CYP3A5			CYP2D6 (strong)	CYP2C19 MBI
	Renal				CYP2D6 competitive
					CYP3A4 competitive
					СҮРЗА4 МВІ
					CYP2C19 competitive (norfluoxetine)
					CYP2C19 MBI (norfluoxetine)
					CYP2D6 competitive (norfluoxetine)
					CYP3A4 competitive (norfluoxetine)
					CYP3A4 MBI (norfluoxetine)
Alprazolam	CYP3A4	NA	Cimetidine	MATE1 inhibition	CYP2D6 competitive
	CYP3A5			MATE2-K inhibition	CYP3A4 competitive
	Renal			OCT2 inhibition	OCT1 Liver competitive
				CYP1A2 (weak)	MATEs Kidney competitive
				CYP2D6 (weak)	OCT2 Kidney competitive
				CYP3A4 (weak)	
Atazanavir	СҮРЗА4	CYP3A4	Ketoconazole	CYP3A4 (strong)	CYP2C8 competitive
	CVD2AF	competitive		Down to be the table of	CVP2CO
	СҮРЗА5	CYP3A5 competitive		P-gp inhibition	CYP2C9 competitive
	Renal	CYP3A4 MBI			CYP3A4 competitive
	HLM - not defined to an	CYP3A5 MBI			CYP3A5 competitive
	enzyme	UGT1A1			
		competitive			
Atazanavir	CYP3A4	CYP3A4	Clarithromycin	CYP3A4 (strong)	CYP3A4 competitive
	CYP3A5	competitive CYP3A5		P-gp inhibition	CYP3A4 MBI
		competitive		. Or	
	Renal	CYP3A4 MBI		OATP1B1 inhibition	OATP1B1 competitive
	HLM - not defined to an enzyme	CYP3A5 MBI		OATP1B3 inhibition	OATP1B3 competitive
	5,	UGT1A1 competitive			P-gp Intestine and Liver competitive

Clarithromycin	СҮРЗА4	CYP3A4 competitive	Atazanavir	OATP1B1/3 inhibition (in combination with ritonavir)	CYP3A4 competitive
	Renal	CYP3A4 MBI			CYP3A5 competitive
		OATP1B1			СҮРЗА4 МВІ
		OATP1B3			СҮРЗА5 МВІ
		P-gp Intestine and			UGT1A1 competitive
		Liver competitive			
Clarithromycin	СҮРЗА4	CYP3A4 competitive	Ritonavir	P-gp inhibition (in combination with saquinavir or lopinavir)	CYP2D6 competitive
	Renal	CYP3A4 MBI		OATP1B1/3 inhibition (in combination with atazanavir	CYP3A4 competitive
		OATP1B1 competitive		or lopinavir) CYP2C9 induction (weak)	CYP3A5 competitive
		OATP1B3		CYP2C19 induction (weak)	СҮРЗА4 МВІ
		competitive P-gp Intestine and Liver competitive		CYP2B6 induction (weak)	СҮРЗА5 МВІ
		,		CYP3A4 (strong)	CYP2C9 induction
					CYP3A4 induction
					CYP3A5 induction
					P-gp Intestine and Liver competitive
Midazolam	СҮРЗА4	NA	Fluconazole	CYP2C9 (moderate)	CYP2C9 competitive
	СҮРЗА5			CYP2C19 (strong)	CYP2C19 competitive
	UGT1A4			CYP3A4 (moderate)	CYP3A4 competitive
	Renal				CYP3A5 competitive
					UGT2B7 competitive
Midazolam	СҮРЗА4	NA	Itraconazole	P-gp inhibition	CYP3A4 competitive
	CYP3A5			CYP3A4 (strong)	OATP1B3 competitive
	UGT1A4				OATP1B1 competitive
	Renal				BCRP competitive
					CYP3A4 competitive (OH-metabolite
					BCRP competitive (OH-metabolite)
					OATP1B3 competitive (OH-metaboli
					OATP1B1 competitive (OH-metabolit

			1		OATP2B1 competitive (OH-metabolite)
					NTCP competitive (OH-metabolite)
Midazolam	СҮРЗА4 СҮРЗА5	NA	Ritonavir	P-gp inhibition (in combination with saquinavir or lopinavir) OATP1B1/3 inhibition (in combination with atazanavir or lopinavir)	CYP3A4 competitive
	UGT1A4			CYP2C9 induction (weak)	CYP3A5 competitive
	Renal			CYP2C19 induction (weak)	СҮРЗА4 МВІ
				CYP2B6 induction (weak)	СҮРЗА5 МВІ
				CYP3A4 (strong)	CYP2C9 induction
					CYP3A4 induction
					CYP3A5 induction
					P-gp Intestine and Liver competitive
Midazolam	СҮРЗА4	NA	Diltiazem	CYP3A4 (moderate)	CYP3A4/5 competitive
	СҮРЗА5				СҮРЗА4/5 МВІ
	UGT1A4				CYP3A4 competitive (metabolite)
	Renal				CYP3A4 MBI (metabolite)
Midazolam	СҮРЗА4	NA	Verapamil	P-gp inhibition	CYP3A4 MBI (norverapamil)
	СҮРЗА5			CYP3A4 (moderate)	CYP3A5 MBI (norverapamil)
	UGT1A4				P-gp competitive (norverepamil)
	Renal				СҮРЗА4 МВІ
					СҮРЗА5 МВІ
					P-gp competitive
Midazolam	СҮРЗА4	NA	Ketoconazole	CYP3A4 (strong)	CYP2C8 competitive
	СҮРЗА5			P-gp inhibition	CYP2C9 competitive
	UGT1A4				CYP3A4 competitive
	Renal				CYP3A5 competitive
Midazolam	СҮРЗА4	NA	Cimetidine	MATE1 inhibition	CYP2D6 competitive
	CYP3A5			MATE2-K inhibition	CYP3A4 competitive
	UGT1A4			OCT2 inhibition	OCT1 Liver competitive
	Renal			CYP1A2 (weak)	MATEs Kidney competitive
				CYP2D6 (weak)	OCT2 Kidney competitive

				CYP3A4 (weak)	
Midazolam	CYP3A4	NA	Erythromycin	CYP3A4 moderate	CYP3A4 competitive
	CYP3A5			P-gp inhibition	СҮРЗА4/5 МВІ
	UGT1A4				
	Renal				
Midazolam	CYP3A4	NA	Fluvoxamine	CYP1A2 (strong)	CYP1A2 competitive
	CYP3A5			CYP2C9 (weak)	CYP2C9 competitive
	UGT1A4			CYP2C19 (strong)	CYP2C19 competitive
	Renal			CYP2D6 (weak)	CYP2D6 competitive
				CYP3A4 (moderate)	CYP3A4/5 competitive
Phenytoin	CYP2C9	CYP2B6 induction	Amiodarone	CYP2C9 (moderate)	CYP2C9 competitive
	CYP2C19	CYP2C9 induction		CYP2D6 (weak)	СҮР2С9 МВІ
	HLM - not defined to an enzyme	CYP3A4 induction		P-gp inhibition	CYP2D6 competitive
	Renal CL	CYP1A2 induction			CYP3A4 competitive
					CYP3A4 MBI
					CYP2C9 competitive (Mono-desethyl- amiodarone) CYP2D6 competitive (Mono-desethyl- amiodarone) CYP2D6 MBI (Mono-desethyl-amiodarone
					CYP3A4 competitive (Mono-desethylamiodarone)
Nifedipine	СҮРЗА4	NA	Cimetidine	MATE1 inhibition	CYP2D6 competitive
	CYP3A5			MATE2-K inhibition	CYP3A4 competitive
	Renal			OCT2 inhibition	OCT1 Liver competitive
				CYP1A2 (weak)	MATEs Kidney competitive
				CYP2D6 (weak)	OCT2 Kidney competitive
				CYP3A4 (weak)	
Nifedipine	СҮРЗА4	NA	Diltiazem	CYP3A4 (moderate)	CYP3A4/5 competitive
	СҮРЗА5				CYP3A4/5 MBI
	Renal				CYP3A4 competitive (metabolite)
					CYP3A4 MBI (metabolite)

Quinidine	СҮРЗА4	CYP2D6	Verapamil	P-gp inhibition	CYP3A4 MBI (norverapamil)
	CYP2C9	competitive CYP3A4		CYP3A4 (moderate)	CYP3A5 MBI (norverapamil)
	CYP2E1	competitive P-gp competitive			P-gp competitive (norverepamil)
	Renal	Oh er here e			CYP3A4 MBI
					СҮРЗА5 МВІ
					P-gp competitive
Quinidine	СҮРЗА4	CYP2D6 competitive	Diltiazem	CYP3A4 (moderate)	CYP3A4/5 competitive
	CYP2C9	CYP3A4 competitive			СҮРЗА4/5 МВІ
	CYP2E1	P-gp competitive			CYP3A4 competitive (metabolite)
	Renal				CYP3A4 MBI (metabolite)
Quinidine	СҮРЗА4	CYP2D6	Cimetidine	MATE1 inhibition	CYP2D6 competitive
	СҮР2С9	competitive CYP3A4 competitive		MATE2-K inhibition	CYP3A4 competitive
	CYP2E1	P-gp competitive		OCT2 inhibition	OCT1 Liver competitive
	Renal			CYP1A2 (weak)	MATEs Kidney competitive
				CYP2D6 (weak)	OCT2 Kidney competitive
				CYP3A4 (weak)	
Quinidine	СҮРЗА4	CYP2D6	Itraconazole	P-gp inhibition	CYP3A4 competitive
	CYP2C9	competitive CYP3A4 competitive		CYP3A4 (strong)	OATP1B3 competitive
	CYP2E1	P-gp competitive			OATP1B1 competitive
	Renal				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)
Quinidine	СҮРЗА4	CYP2D6 competitive	Erythromycin	CYP3A4 moderate	CYP3A4 competitive

	CYP2C9 CYP2E1 Renal	CYP3A4 competitive P-gp competitive		P-gp inhibition	CYP3A4/5 MBI
Quinidine	СҮРЗА4	CYP2D6	Fluvoxamine	CYP1A2 (strong)	CYP1A2 competitive
	СҮР2С9	competitive CYP3A4 competitive		CYP2C9 (weak)	CYP2C9 competitive
	CYP2E1	P-gp competitive		CYP2C19 (strong)	CYP2C19 competitive
	Renal			CYP2D6 (weak)	CYP2D6 competitive
				CYP3A4 (moderate)	CYP3A4/5 competitive
Repaglinide	CYP2C8	NA	Itraconazole	P-gp inhibition	CYP3A4 competitive
	СҮРЗА4			CYP3A4 (strong)	OATP1B3 competitive
	Renal				OATP1B1 competitive
	OATP1B1				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	NA	Cyclosporine	P-gp inhibition	CYP3A4 competitive
	CYP3A4			BCRP inhibition	P-gp competitive
	Renal			OATP1B1 inhibition	BCRP competitive
	OATP1B1			OATP1B3 inhibition	NTCP competitive
				CYP3A4 (moderate)	OATP1B1 competitive
					OATP1B3 competitive
					OATP2B1 competitive
Repaglinide	CYP2C8	NA	Clarithromycin	CYP3A4 (strong)	CYP3A4 competitive
	СҮРЗА4			P-gp inhibition	СҮРЗА4 МВІ
	Renal			OATP1B1 inhibition	OATP1B1 competitive
	OATP1B1			OATP1B3 inhibition	OATP1B3 competitive
					P-gp Intestine and Liver competitive

Sildenafil	CYP2C9	NA	Clarithromycin	CYP3A4 (strong)	CYP3A4 competitive
	СҮРЗА4			P-gp inhibition	СҮРЗА4 МВІ
	Renal CL			OATP1B1 inhibition	OATP1B1
				OATP1B3 inhibition	OATP1B3
					P-gp Intestine and Liver competitive
Sildenafil	CYP2C9	NA	Erythromycin	CYP3A4 moderate	CYP3A4 competitive
	СҮРЗА4			P-gp inhibition	CYP3A4/5 MBI
	Renal CL				
Sildenafil	CYP2C9	NA	Ritonavir	P-gp inhibition (in combination	CYP2D6 competitive
	СҮРЗА4			with saquinavir or lopinavir) OATP1B1/3 (in combination	CYP3A4 competitive
	CIFJA4			with atazanavir or lopinavir)	CIT 3A4 competitive
	Renal CL			CYP2C9 induction (weak)	CYP3A5 competitive
				CYP2C19 induction (weak)	СҮРЗА4 МВІ
				CYP2B6 induction (weak)	СҮРЗА5 МВІ
				CYP3A4 (strong)	CYP2C9 induction
					CYP3A4 induction
					CYP3A5 induction
					P-gp Intestine and Liver competitive
Sildenafil	CYP2C9	NA	Cimetidine	MATE1 inhibition	CYP2D6 competitive
	CYP3A4			MATE2-K inhibition	CYP3A4 competitive
	Renal CL			OCT2 inhibition	OCT1 Liver competitive
				CYP1A2 (weak)	MATEs Kidney competitive
				CYP2D6 (weak)	OCT2 Kidney competitive
				CYP3A4 (weak)	
Simvastatin	СҮРЗА4	NA	Diltiazem	CYP3A4 (moderate)	CYP3A4/5 competitive
	HLM - not defined to an				СҮРЗА4/5 МВІ
	enzyme HIMms - not defined to an				CVD2A4 compatitive (matchelite)
	enzyme				CYP3A4 competitive (metabolite)
					CYP3A4 MBI (metabolite)
Simvastatin	СҮРЗА4	NA	Erythromycin	CYP3A4 moderate	CYP3A4 competitive
	HLM - not defined to an enzyme			P-gp inhibition	CYP3A4/5 MBI

	HIMms - not defined to an enzyme				
Simvastatin	СҮРЗА4	NA	Verapamil	P-gp inhibition	CYP3A4 MBI (norverapamil)
	HLM - not defined to an			CYP3A4 (moderate)	CYP3A5 MBI (norverapamil)
	enzyme				P-gp competitive (norverepamil)
	HIMms - not defined to an				СҮРЗА4 МВІ
	enzyme				СҮРЗА5 МВІ
					P-gp competitive
Simvastatin	СҮРЗА4	NA	Ketoconazole	CYP3A4 (strong)	CYP2C8 competitive
	HLM - not defined to an			P-gp inhibition	CYP2C9 competitive
	enzyme HIMms - not defined to an enzyme				CYP3A4 competitive
	Chizyme				CYP3A5 competitive
Simvastatin	СҮРЗА4	NA	Clarithromycin	CYP3A4 (strong)	CYP3A4 competitive
	HLM - not defined to an			P-gp inhibition	СҮРЗА4 МВІ
	enzyme			OATP1B1 inhibition	OATP1B1 competitive
	HIMms - not defined to an			OATP1B3 inhibition	OATP1B3 competitive
	enzyme				P-gp Intestine and Liver competitive
Triazolam	СҮРЗА4	NA	Diltiazem	CYP3A4 (moderate)	CYP3A4/5 competitive
	СҮРЗА5				CYP3A4/5 MBI
	Renal				CYP3A4 competitive (metabolite)
					CYP3A4 MBI (metabolite)
Triazolam	CYP3A4	NA	Fluconazole	CYP2C9 (moderate)	CYP2C9 competitive
	СҮРЗА5			CYP2C19 (strong)	CYP2C19 competitive
	Renal			CYP3A4 (moderate)	CYP3A4 competitive
					CYP3A5 competitive
					UGT2B7 competitive
Triazolam	СҮРЗА4	NA	Ketoconazole	CYP3A4 (strong)	CYP2C8 competitive
	СҮРЗА5			P-gp inhibition	CYP2C9 competitive
	Renal				CYP3A4 competitive
					CYP3A5 competitive
Triazolam	СҮРЗА4	NA	Clarithromycin	CYP3A4 (strong)	CYP3A4 competitive

	CYP3A5			P-gp inhibition	CYP3A4 MBI
	Renal			OATP1B1 inhibition	OATP1B1 competitive
				OATP1B3 inhibition	OATP1B3 competitive
					P-gp Intestine and Liver competitive
Triazolam	СҮРЗА4	NA	Cimetidine	MATE1 inhibition	CYP2D6 competitive
	CYP3A5			MATE2-K inhibition	CYP3A4 competitive
	Renal			OCT2 inhibition	OCT1 Liver competitive
				CYP1A2 (weak)	MATEs Kidney competitive
				CYP2D6 (weak)	OCT2 Kidney competitive
				CYP3A4 (weak)	
Triazolam	СҮРЗА4	NA	Erythromycin	CYP3A4 moderate	CYP3A4 competitive
	СҮРЗА5			P-gp inhibition	СҮРЗА4/5 МВІ
	Renal				
Triazolam	СҮРЗА4	NA	Itraconazole	P-gp inhibition	CYP3A4 competitive
	CYP3A5			CYP3A4 (strong)	OATP1B3 competitive
	Renal				OATP1B1 competitive
					BCRP competitive
					CYP3A4 competitive (OH-metabolite
					BCRP competitive (OH-metabolite)
					OATP1B3 competitive (OH-metabolite
					OATP1B1 competitive (OH-metabolit
					OATP2B1 competitive (OH-metabolit
					NTCP competitive (OH-metabolite)
Zolpidem	CYP1A2	NA	Itraconazole	P-gp inhibition	CYP3A4 competitive
	CYP2C9			CYP3A4 (strong)	OATP1B3 competitive
	CYP2C19				OATP1B1 competitive
	CYP2D6				BCRP competitive
	СҮРЗА4				CYP3A4 competitive (OH-metabolite
					BCRP competitive (OH-metabolite)
					OATP1B3 competitive (OH-metabolit
					OATP1B1 competitive (OH-metabolit
					OATP2B1 competitive (OH-metabolite

					NTCP competitive (OH-metabolite)
S-Warfarin	Renal	NA	Fluconazole	CYP2C9 (moderate)	CYP2C9 competitive
	CYP2C9 (allelics)			CYP2C19 (strong)	CYP2C19 competitive
				CYP3A4 (moderate)	CYP3A4 competitive
					CYP3A5 competitive
					UGT2B7 competitive
Tolbutamide	CYP2C9	NA	Fluconazole	CYP2C9 (moderate)	CYP2C9 competitive
	CYP2C19			CYP2C19 (strong)	CYP2C19 competitive
	Renal			CYP3A4 (moderate)	CYP3A4 competitive
					CYP3A5 competitive
					UGT2B7 competitive
Phenytoin	CYP2C9	CYP2B6 induction	Fluconazole	CYP2C9 (moderate)	CYP2C9 competitive
	CYP2C19	CYP2C9 induction		CYP2C19 (strong)	CYP2C19 competitive
	HLM - not defined to an enzyme	CYP3A4 induction		CYP3A4 (moderate)	CYP3A4 competitive
	Renal CL	CYP1A2 induction			CYP3A5 competitive
					UGT2B7 competitive
Celecoxib	CYP2C9 (allelics)	NA	Fluconazole	CYP2C9 (moderate)	CYP2C9 competitive
	СҮРЗА4			CYP2C19 (strong)	CYP2C19 competitive
	HLM - not defined to an enzyme			CYP3A4 (moderate)	CYP3A4 competitive
	Renal CL				CYP3A5 competitive
					UGT2B7 competitive
Tolbutamide	CYP2C9	NA	Fluvoxamine	CYP1A2 (strong)	CYP1A2 competitive
	CYP2C19			CYP2C9 (weak)	CYP2C9 competitive
	Renal			CYP2C19 (strong)	CYP2C19 competitive
				CYP2D6 (weak)	CYP2D6 competitive
				CYP3A4 (moderate)	CYP3A4/5 competitive
Phenytoin	CYP2C9	CYP2B6 induction	Sulphaphenazole	NA - in vivo	CYP2C9 competitive
	CYP2C19	CYP2C9 induction			CYP2C19 competitive
	HLM - not defined to an enzyme	CYP3A4 induction			
	Renal CL	CYP1A2 induction			

Tolbutamide	СҮР2С9	NA	Sulphaphenazole	NA - in vivo	CYP2C9 competitive
	CYP2C19				CYP2C19 competitive
	Renal				
Atomoxetine	CYP2D6	NA	Fluvoxamine	CYP1A2 (strong)	CYP1A2 competitive
	CYP2C19			CYP2C9 (weak)	CYP2C9 competitive
	HLM - not defined to an			CYP2C19 (strong)	CYP2C19 competitive
	enzyme			CYP2D6 (weak)	CYP2D6 competitive
	Renal Cl			CYP3A4 (moderate)	CYP3A4/5 competitive
Atomoxetine	CYP2D6	NA	Paroxetine	CYP2D6 (strong)	CYP2D6 competitive
	CYP2C19				CYP3A4 competitive
	HLM - not defined to an enzyme				CYP2D6 (MBI)
	Renal Cl				CYP3A4 (MBI)
Desipramine	Renal CL	NA	Paroxetine	CYP2D6 (strong)	CYP2D6 competitive
	CYP2D6				CYP3A4 competitive
	cytosol- not defined to an enzyme				CYP2D6 (MBI)
					СҮРЗА4 (МВІ)
Desipramine	Renal CL	NA	Fluoxetine	CYP2C19 (strong)	CYP2C19 competitive
	CYP2D6			CYP2D6 (strong)	CYP2C19 MBI
	cytosol- not defined to an enzyme				CYP2D6 competitive
					CYP3A4 competitive
					СҮРЗА4 МВІ
					CYP2C19 competitive (norfluoxetine)
					CYP2C19 MBI (norfluoxetine)
					CYP2D6 competitive (norfluoxetine)
					CYP3A4 competitive (norfluoxetine)
					CYP3A4 MBI (norfluoxetine)
Desipramine	Renal CL	NA	Bupropion	CYP2D6 (strong)	CYP2D6 competitive
	CYP2D6				CYP2D6 competitive (metabolite)
	cytosol- not defined to an enzyme				

Desipramine	Renal CL CYP2D6 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)	CYP2D6 competitive 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 CYP2D6 CYP3A4 Renal CI	NA	Quinidine	CYP2D6 (strong) P-gp inhibition	CYP2D6 competitive CYP3A4 competitive P-gp competitive
Dextromethorphan	CYP2B6 CYP2C9 CYP2C18 CYP2C19 CYP2D6 CYP3A4 Renal CI	NA	Fluoxetine	CYP2C19 (strong) CYP2D6 (strong)	CYP2C19 competitive CYP2C19 MBI CYP2D6 competitive CYP3A4 competitive CYP3A4 MBI CYP2C19 competitive (norfluoxetine) CYP2C19 MBI (norfluoxetine) CYP2D6 competitive (norfluoxetine) CYP3A4 competitive (norfluoxetine) CYP3A4 MBI (norfluoxetine)
Metoprolol	CYP2D6 CYP3A4 Renal Cl	NA	Paroxetine	CYP2D6 (strong)	CYP2D6 competitive CYP3A4 competitive CYP2D6 (MBI)

					СҮРЗА4 (МВІ)
Metoprolol	CYP2D6	NA	Quinidine	CYP2D6 (strong)	CYP2D6 competitive
	СҮРЗА4			P-gp inhibition	CYP3A4 competitive
	Renal Cl				P-gp competitive
Tolterodine	CYP2D6	NA	Fluoxetine	CYP2C19 (strong)	CYP2C19 competitive
	СҮРЗА4			CYP2D6 (strong)	CYP2C19 MBI
	Renal Cl				CYP2D6 competitive
					CYP3A4 competitive
					СҮРЗА4 МВІ
					CYP2C19 competitive (norfluoxetine)
					CYP2C19 MBI (norfluoxetine)
					CYP2D6 competitive (norfluoxetine)
					CYP3A4 competitive (norfluoxetine)
					CYP3A4 MBI (norfluoxetine)
Repaglinide	CYP2C8	NA	Trimethoprim	CYP2C8 (weak)	CYP2C8 competitive
	CYP3A4				OCT2 Kidney competitive
	Renal				MATEs Kidney competitive
	OATP1B1				OCT1 Liver competitive
Repaglinide	CYP2C8	NA	Gemfibrozil	OATP1B1 inhibition	CYP2C8 competitive
	CYP3A4			OATP1B3 inhibition	CYP2C9 competitive
	Renal			CYP2C8 (strong)	OAT3 Kidney competitive
	OATP1B1				OATP1B1 competitive
					OATP1B3 competitive
					OAT3 Kidney competitive (metabolite)
					OATP1B1 competitive (metabolite)
					CYP2C8 competitive (metabolite)
					CYP2C8 MBI (metabolite)
Rosiglitazone	CYP2C8	NA	Trimethoprim	CYP2C8 (weak)	CYP2C8 competitive
	CYP2C9				OCT2 Kidney competitive
	HLM - not defined to an				MATEs
	enzyme				OCT1 Liver competitive
					OCTI Liver competitive

Rosiglitazone	CYP2C8	NA	Gemfibrozil	OATP1B1 inhibition	CYP2C8 competitive
	CYP2C9			OATP1B3 inhibition	CYP2C9 competitive
	HLM - not defined to an enzyme			CYP2C8 (strong)	OAT3 Kidney competitive
					OATP1B1 competitive
					OATP1B3 competitive
					OAT3 Kidney competitive (metabolite)
					OATP1B1 competitive (metabolite)
					CYP2C8 competitive (metabolite)
					CYP2C8 MBI (metabolite)
Caffeine	CYP1A2	NA	Ciprofloxacin	CYP1A2 (strong)	CYP1A2 competitive
	CYP2E1			CYP3A4 (moderate)	CYP3A4 competitive
	Renal CL				
Caffeine	CYP1A2	NA	Fluvoxamine	CYP1A2 (strong)	CYP1A2 competitive
	CYP2E1			CYP2C9 (weak)	CYP2C9 competitive
	Renal CL			CYP2C19 (strong)	CYP2C19 competitive
				CYP2D6 (weak)	CYP2D6 competitive
				CYP3A4 (moderate)	CYP3A4/5 competitive
Theophylline	CYP1A2	NA	Ciprofloxacin	CYP1A2 (strong)	CYP1A2 competitive
	CYP2D6			CYP3A4 (moderate)	CYP3A4 competitive
	СҮРЗА4				
	CYP2E1				
	Renal Cl				
Theophylline	CYP1A2	NA	Fluvoxamine	CYP1A2 (strong)	CYP1A2 competitive
	CYP2D6			CYP2C9 (weak)	CYP2C9 competitive
	СҮРЗА4			CYP2C19 (strong)	CYP2C19 competitive
	CYP2E1			CYP2D6 (weak)	CYP2D6 competitive
	Renal Cl			CYP3A4 (moderate)	CYP3A4/5 competitive
S-Mephenytoin	CYP2C9	NA	Fluvoxamine	CYP1A2 (strong)	CYP1A2 competitive
	CYP2C19			CYP2C9 (weak)	CYP2C9 competitive
	Renal Cl			CYP2C19 (strong)	CYP2C19 competitive
				CYP2D6 (weak)	CYP2D6 competitive

				CYP3A4 (moderate)	CYP3A4/5 competitive
Omeprazole	CYP2C19	CYP2C19 MBI	Fluvoxamine	CYP1A2 (strong)	CYP1A2 competitive
	СҮРЗА4	CYP1A2 induction		CYP2C9 (weak)	CYP2C9 competitive
				CYP2C19 (strong)	CYP2C19 competitive
				CYP2D6 (weak)	CYP2D6 competitive
				CYP3A4 (moderate)	CYP3A4/5 competitive
Omeprazole	CYP2C19	CYP2C19 MBI	Fluoxetine	CYP2C19 (strong)	CYP2C19 competitive
	СҮРЗА4	CYP1A2 induction		CYP2D6 (strong)	CYP2C19 MBI
					CYP2D6 competitive
					CYP3A4 competitive
					СҮРЗА4 МВІ
					CYP2C19 competitive (norfluoxetin
					CYP2C19 MBI (norfluoxetine)
					CYP2D6 competitive (norfluoxetine)
					CYP3A4 competitive (norfluoxetine
					CYP3A4 MBI (norfluoxetine)
Imipramine	CYP1A2	NA	Fluoxetine	CYP2C19 (strong)	CYP2C19 competitive
	CYP2C19			CYP2D6 (strong)	CYP2C19 MBI
	CYP2D6				CYP2D6 competitive
	СҮРЗА4				CYP3A4 competitive
	HLM - not defined to an enzyme				СҮРЗА4 МВІ
	Renal Cl				CYP2C19 competitive (norfluoxeting
					CYP2C19 MBI (norfluoxetine)
					CYP2D6 competitive (norfluoxetine
					CYP3A4 competitive (norfluoxetine
					CYP3A4 MBI (norfluoxetine)
Omeprazole	CYP2C19	CYP2C19 MBI	Ticlopidine	CYP2B6 (weak)	CYP2B6 (MBI)
	CYP3A4	CYP1A2 induction		CYP2C19 (strong)	CYP2C19 (MBI)
Tizanidine	CYP1A2	NA	Fluvoxamine	CYP1A2 (strong)	CYP1A2 competitive
	Renal Cl			CYP2C9 (weak)	CYP2C9 competitive
				CYP2C19 (strong)	CYP2C19 competitive

				CYP2D6 (weak)	CYP2D6 competitive
				CYP3A4 (moderate)	CYP3A4/5 competitive
Tizanidine	CYP1A2	NA	Ciprofloxacin	CYP1A2 (strong)	CYP1A2 competitive
	Renal CL			CYP3A4 (moderate)	CYP3A4 competitive
Aprepitant	СҮРЗА4	CYP3A4 induction	Ketoconazole	CYP3A4 (strong)	CYP2C8 competitive
	HLM - not defined to an enzyme	CYP3A4 inhibition		P-gp inhibition	CYP2C9 competitive
	Additional systemic clearance	CYP3A4 MBI			CYP3A4 competitive
		CYP2C9 induction			CYP3A5 competitive
Dexamethasone	СҮРЗА4	CYP3A4 induction	Itraconazole	P-gp inhibition	CYP3A4 competitive
	HLM - not defined to an enzyme			CYP3A4 (strong)	OATP1B3 competitive
	Renal CL				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	СҮРЗА4	CYP3A4 induction	Aprepitant	CYP3A4 (moderate)	CYP3A4 competitive
	HLM - not defined to an			CYP2C9 induction (weak)	СҮРЗА4 МВІ
	enzyme				CYP2C9 induction
	Renal CL				CYP3A4 induction
Ibrutinib	СҮРЗА4	NA	Ketoconazole	CYP3A4 (strong)	CYP2C8 competitive
	HLM - not defined to an enzyme			P-gp inhibition	CYP2C9 competitive
	Renal CL				CYP3A4 competitive
					CYP3A5 competitive
Ibrutinib	СҮРЗА4	NA	Itraconazole	CYP3A4 (strong)	CYP3A4 competitive
	HLM - not defined to an enzyme			P-gp inhibition	OATP1B3 competitive
	Renal CL				OATP1B1 competitive

					BCRP competitive
					CYP3A4 competitive (OH-metabolit
					BCRP competitive (OH-metabolite)
					OATP1B3 competitive (OH-metaboli
					OATP1B1 competitive (OH-metaboli
					OATP2B1 competitive (OH-metaboli
					NTCP competitive (OH-metabolite)
Midazolam	СҮРЗА4	NA	Aprepitant	CYP3A4 (moderate)	CYP3A4 competitive
	CYP3A5			CYP2C9 induction (weak)	СҮРЗА4 МВІ
	UGT1A4				CYP3A4 induction
	Renal CL				CYP2C9 induction
Rifabutin	СҮРЗА4	CYP2J2 induction	Fluconazole	CYP2C9 (moderate)	CYP2C9 competitive
	CYP2J2	CYP3A4 induction		CYP2C19 (strong)	CYP2C19 competitive
	Renal CL	CYP3A5 induction		CYP3A4 (moderate)	CYP3A4 competitive
					CYP3A5 competitive
					UGT2B7 competitive
Rifabutin	СҮРЗА4	CYP2J2 induction	Ritonavir	P-gp inhibition (in combination	CYP2D6 competitive
	CYP2J2	CYP3A4 induction		with saquinavir or lopinavir) OATP1B1/3 (in combination	CYP3A4 competitive
	CTF 2J2	CIF SA4 illudetion		with atazanavir or lopinavir)	CIPSA4 competitive
	Renal CL	CYP3A5 induction		CYP2C9 induction (weak)	CYP3A5 competitive
				CYP2C19 induction (weak)	СҮРЗА4 МВІ
				CYP2B6 induction (weak)	СҮРЗА5 МВІ
				CYP3A4 (strong)	CYP2C9 induction
					CYP3A4 induction
					CYP3A5 induction
					P-gp Intestine and Liver competitive
Rifabutin	СҮРЗА4	CYP2J2 induction	Clarithromycin	CYP3A4 (strong)	CYP3A4 competitive
	CYP2J2	CYP3A4 induction		P-gp inhibition	СҮРЗА4 МВІ
	Renal CL	CYP3A5 induction		OATP1B1	OATP1B1
				OATP1B3	OATP1B3
					P-gp Intestine and Liver competitive
Simvastatin	CYP3A4	NA	Amiodarone	CYP2C9 (moderate)	CYP2C9 competitive

	HLM - not defined to an enzyme			CYP2D6 (weak)	CYP2C9 MBI
	HIMms - not defined to an enzyme			P-gp inhibition	CYP2D6 competitive
	enzyme				CYP3A4 competitive
					СҮРЗА4 МВІ
					CYP2C9 competitive (Mono-desethyl- amiodarone) CYP2D6 competitive (Mono-desethyl- amiodarone) CYP2D6 MBI (Mono-desethyl-amiodarone)
					CYP3A4 competitive (Mono-desethyl- amiodarone)
Flurbiprofen	CYP2C9 (allelics)	NA	Fluconazole	CYP2C9 (moderate)	CYP2C9 competitive
	UGT2B7			CYP2C19 (strong)	CYP2C19 competitive
				CYP3A4 (moderate)	CYP3A4 competitive
					CYP3A5 competitive
					UGT2B7 competitive
S-Warfarin	Renal	NA	Amiodarone	CYP2C9 (moderate)	CYP2C9 competitive
	CYP2C9 (allelics)			CYP2D6 (weak)	СҮР2С9 МВІ
				P-gp inhibition	CYP2D6 competitive
					CYP3A4 competitive
					CYP3A4 MBI
					CYP2C9 competitive (metabolite)
					CYP2D6 competitive (metabolite)
					CYP2D6 MBI (metabolite)
					CYP3A4 competitive (metabolite)
Desipramine	CYP2D6	NA	Cinacalcet	CYP2D6 (moderate)	CYP2D6 competitive
	Renal CL				
	cytosol- not defined to an enzyme				
Nebivolol	СҮРЗА4	NA	Paroxetine	CYP2D6 (strong)	CYP2D6 competitive
	CYP2D6				CYP3A4 competitive
	HLM - not defined to an enzyme				CYP2D6 (MBI)

					СҮРЗА4 (МВІ)
Nebivolol	CYP3A4	NA	Bupropion	CYP2D6 (strong)	CYP2D6 competitive
	CYP2D6				CYP2D6 competitive (metabolite)
	HLM - not defined to an enzyme				
Nebivolol	CYP3A4	NA	Fluvoxamine	CYP1A2 (strong)	CYP1A2 competitive
	CYP2D6			CYP2C9 (weak)	CYP2C9 competitive
	HLM - not defined to an enzyme			CYP2C19 (strong)	CYP2C19 competitive
	·			CYP2D6 (weak)	CYP2D6 competitive
				CYP3A4 (moderate)	CYP3A4/5 competitive
Nebivolol	СҮРЗА4	NA	Fluoxetine	CYP2C19 (strong)	CYP2C19 competitive
	CYP2D6			CYP2D6 (strong)	CYP2C19 MBI
	HLM - not defined to an				CYP2D6 competitive
	enzyme				CYP3A4 competitive
					СҮРЗА4 МВІ
					CYP2C19 competitive (norfluoxetine)
					CYP2C19 MBI (norfluoxetine)
					CYP2D6 competitive (norfluoxetine)
					CYP3A4 competitive (norfluoxetine)
					CYP3A4 MBI (norfluoxetine)