	Substrate	CYP450 and UGT		Transporters	
		Inhibitor	Inducer	Inhibitor	Inducer
Tenofovir alafenamide ¹	P-gp, BCRP; minimal metabolism via 3A4	3A4 (weak – in vitro only; not an inhibitor in vivo). Does not inhibit CYP1A2, 2B6, 2C8, 2C9, 2C19, 2D6 or UGT1A.	Not an inducer of 3A4 in vivo.		
HIV PIs					
atazanavir ²	Mainly CYP3A P-gp, MRP1	3A4, UGT1A1 >> 2C8 (weak)* *Caution when unboosted atazanavir is coadministered with 2C8 substrates with narrow therapeutic indices (e.g., paclitaxel, repaglinide); clinically significant interactions with 2C8 substrates are not expected when atazanavir is boosted with ritonavir.		P-gp, MRP1, OATP1B1, OATP1B3, BCRP	
darunavir ³	Mainly CYP3A, P-gp	CYP3A4			
fosamprenavir ⁴ , indinavir ⁵ , lopinavir/ritonavir ⁶ , saquinavir ⁷	Mainly CYP3A, P-gp, MRP1 (LPV, SQV)	CYP3A4 (saquinavir is a weak inhibitor)		P-gp (LPV) OATP1B1, OATP1B3 (LPV, SQV)	
nelfinavir ⁸	Mainly CYP3A, 2C19, P-gp	CYP3A4	UGT, 2B6, 2C8, 2C9/19 ⁹		
tipranavir ¹⁰	Mainly CYP3A, P-gp	2D6 ¹¹	CYP3A4 (potent) ¹⁰ , UGT	OATP1B1	P-gp
PK Boosters					
ritonavir ¹²	CYP3A4, P-gp, MRP1	CYP3A4 (potent)> >2D6* >2C9 >2C19 >2A6 >1A2>2E1. *negligible effect at boosting doses ⁶	UGT, CYP1A2, CYP2C9/19, 2B6 (inhibits in vitro, ¹³ but induces in vivo ¹⁴)	P-gp, OATP1B1, OATP1B3, BCRP, OATP2B1, OCT2	
cobicistat	CYP3A, 2D6 (minor)	CYP3A, CYP2D6		P-gp, BCRP, OATP1B1 and OATP1B3, MATE1	
HIV NNRTIs					
delavirdine ¹⁵	CYP3A4	3A4 (potent)			
doravirine (MK-1439)	CYP3A4/5. Not a substrate of OATP1B1	Does not inhibit CYP3A4, 2D6, 1A2, 2B6, 2C8/9, 2C19, or UGT	Unlikely to induce CYP enzymes to a clinically relevant extent.	Not anticipated to inhibit OATP1B1/3, OAT1, OAT3, OCT2, BCRP in a clinically relevant manner.	

	Substrate	CYP450 and UGT		Transporters	
		Inhibitor	Inducer	Inhibitor	Inducer
efavirenz ¹⁶	CYP3A4, 2B6 (minor)	2C9, 2C19 ¹⁶ (? Clinical significance).	3A4 (potent), 2B6 ¹⁷ , UGT1A1 ¹⁸		
etravirine ¹⁹	CYP3A4, CYP2C9, and CYP2C19	CYP2C9 (weak), CYP2C19 (moderate), p-glycoprotein (weak)	3A4 (weak)		
nevirapine ²⁰	CYP3A4, 2B6 (minor)		3A4, 2B6 (potent)		
rilpivirine ²¹	CYP3A4 (major), as well as CYP2C19, 1A2, 2C8/9/10 (minor).		2C19 (moderate), CYP1A2, 2B6 and 3A4 (weak). ²² A clinically relevant effect on CYP enzyme activity is considered unlikely with the 25 mg dose. ²¹	OCT2	
HIV INSTIS					
dolutegravir ²³	UGT1A1, CYP3A4 (10-15%); not a substrate of OATP1B1 or 1B3.		Does not induce CYP1A2, CYP2B6, or CYP3A4 in vitro.	OCT2	
elvitegravir ²⁴	CYP3A4		CYP2C9 (modest)		
raltegravir ²⁵	UGT1A1	Raltegravir has no inhibitory or inductive potential in vitro.	Raltegravir has no inhibitory or inductive potential in vitro.		
HIV CCR5 INHIBITOR	RS				
cenicriviroc ²⁶	CYP3A4, 2C8. Not a substrate of OATP1B1/B3 or OCT2.	Not a known CYP inhibitor.	Not a known CYP inducer.	P-gp Not an inhibitor of OATP1B1/B3 or OCT2.	
maraviroc ²⁷	CYP3A4, P-gp	Does not inhibit major CYP isozymes at clinically relevant concentrations.		P-gp (in gut; systemic effects unlikely).	
HIV ATTACHMENT II	NHIBITOR				
BMS 663068 (prodrug of 626529)	CYP3A4 (partial)	Not anticipated to inhibit UGT1A1, 1A4, 1A9 or CYP450 enzymes.	No CYP3A4 induction.	Inhibitor of OATP1B3. Not anticipated to inhibit other transporters including OCT2, OAT1, OAT3, MATE1, MRP2, BSEP, NTCP and P-gp.	

	Substrate	CYP450 and UGT		Transporters	
		Inhibitor	Inducer	Inhibitor	Inducer
CO-FORMULATED/C	OMBINATION HCV REG	IMENS			
Epclusa®					
velpatasvir ^{28, 29}	CYP3A4, 2C8, 2B6; OATP1B1, OATP1B3, P-gp, BCRP.	No inhibiting or inducing effects on P450.	No inhibiting or inducing effects on P450.	P-gp (weak), OATP1B1, 1B3, 2B1 (weak), BCRP (moderate).	
sofosbuvir ³⁰	P-gp, BCRP.GS- 331007 (primary systemic nucleoside metabolite, accounts for >90% of systemic drug exposure): not a P-gp substrate	No inhibiting or inducing effects on P450 and UGT1A1.	No inhibiting or inducing effects on P450 and UGT1A1.	No inhibiting or inducing effects on P-gp, BCRP, OATP1B1, OATP1B3, OCT1, BSEP.	No inhibiting or inducing effects on P-gp, BCRP, OATP1B1, OATP1B3, OCT1, BSEP.
Harvoni®					
ledipasvir ³¹	P-gp (likely)	Not an inhibitor or inducer of P450 or UGT.	Not an inhibitor or inducer of P450 or UGT.	Weak inhibitor of P-gp and BRCP (intestinal, not systemic). Likely a weak inhibitor of OATP1B1/1B3.	
sofosbuvir ³⁰	P-gp, BCRP.GS- 331007 (primary systemic nucleoside metabolite, accounts for >90% of systemic drug exposure): not a P-gp substrate	No inhibiting or inducing effects on P450 and UGT1A1.	No inhibiting or inducing effects on P450 and UGT1A1.	No inhibiting or inducing effects on P-gp, BCRP, OATP1B1, OATP1B3, OCT1, BSEP.	No inhibiting or inducing effects on P-gp, BCRP, OATP1B1, OATP1B3, OCT1, BSEP.
Holkira Pak® ^{32, 33}					
paritaprevir (NS3/4A PI)	3A4, P-gp, OATP1B1, OATP1B3, BCRP.	UGT1A1 (net effect of 3D is UGT1A1 inhibition) ³⁴		OATP1B1 and OATP1B3; P-gp, BCRP (potential).	
ombitasvir (NS5A inhibitor)	3A4, P-gp, BCRP.	UGT1A1 (net effect of 3D is UGT1A1 inhibition) ³⁴			
dasabuvir (NS5B inhibitor)	CYP2C8>3A4, P-gp, BCRP.	UGT1A1 (net effect of 3D is UGT1A1 inhibition) ³⁴		BCRP, P-gp (potential)	
ritonavir ¹²	CYP3A4, P-gp, MRP1	CYP3A4 (potent)> >2D6* >2C9 >2C19 >2A6 >1A2>2E1. *negligible effect at boosting	UGT, CYP1A2, CYP2C9/19, 2B6 (inhibits in vitro, ¹³ but induces in vivo ¹⁴)	P-gp, OATP1B1, OATP1B3, BCRP, OATP2B1, OCT2	

	Substrate	CYP450 and UGT		Transporters	
		Inhibitor	Inducer	Inhibitor	Inducer
		doses ⁶			
Zepatier® ³⁵					
elbasvir ^{36, 37} (NS5A inhibitor)	CYP3A4, P-glycoprotein (P-gp) and OATP in vitro.	Does not inhibit CYP3A4	Does not induce CYP1A2, 2B6 or 3A4. ³⁵	BCRP (intestinal) ³⁵ , P-gp (in vitro only; not expected to cause clinically significant interactions via P-gp inhibition at usual clinical doses) ³⁸ Does not inhibit OATP1B ³⁵	
grazoprevir ^{37, 39} (NS3/4A PI)	CYP3A4, P-gp and OATP1B1	CYP2C8 (not clinically meaningful), 40 3A4 (weak), UGT1A1 (weak)	Does not induce CYP1A2, 2B6 or 3A4. ³⁵	BCRP (intestinal) ³⁵ . Does not inhibit OATP1B ³⁵	
SOF/VEL/VOX					
sofosbuvir ³⁰	P-gp, BCRP.GS- 331007 (primary systemic nucleoside metabolite, accounts for >90% of systemic drug exposure): not a P-gp substrate	No inhibiting or inducing effects on P450 and UGT1A1.	No inhibiting or inducing effects on P450 and UGT1A1.	No inhibiting or inducing effects on P-gp, BCRP, OATP1B1, OATP1B3, OCT1, BSEP.	No inhibiting or inducing effects on P-gp, BCRP, OATP1B1, OATP1B3, OCT1, BSEP.
velpatasvir ^{28, 29}	CYP3A4, 2C8, 2B6; OATP1B1, OATP1B3, P-gp, BCRP.	No inhibiting or inducing effects on P450.	No inhibiting or inducing effects on P450.	P-gp (weak), OATP1B1, 1B3, 2B1 (weak), BCRP (moderate).	
voxilaprevir (GS- 9857) ⁴¹	CYP3A4, 2C8, P-gp, BCRP, OATPs			P-gp, BCRP, OATPs	
Daclatasvir-TRIO					
asunaprevir (NS3 PI) ⁴² , ⁴³	CYP3A4, P-gp; OATP1B/2B1	CYP2D6 (moderate)	CYP3A4 (weak)	P-gp, OATP1B1/2B1 (weak)	
beclabuvir ^{44, 45} (NS5B inhibitor)	CYP3A4, P-gp; OATP1B1/1B3		CYP3A4 (weak- moderate); 46-50% ↓ midazolam AUC	P-gp	
daclatasvir ⁴⁶ (NS5A inhibitor)	CYP3A4, P-gp, OCT1. (*inhibition of P-gp alone with no/minimal CYP3A4		CYP3A4 (weak; no meaningful effect on midazolam kinetics)	P-gp (weak-moderate), weak inhibitor of OATP1B1, OCT1, and BCRP.	

	Substrate	CYP450 and UGT		Transporters	
		Inhibitor	Inducer	Inhibitor	Inducer
	inhibition not expected to significantly increase daclatasvir exposure)				
HCV NS5A INHIBIT	TORS				
daclatasvir ⁴⁶	CYP3A4, P-gp, OCT1. (*inhibition of P-gp alone with no/minimal CYP3A4 inhibition not expected to significantly increase daclatasvir exposure)		CYP3A4 (weak; no meaningful effect on midazolam kinetics)	P-gp (weak-moderate), weak inhibitor of OATP1B1, OCT1, and BCRP.	
elbasvir ^{36, 37}	CYP3A4, P- glycoprotein (P-gp) and OATP in vitro.	Does not inhibit CYP3A4	Does not induce CYP1A2, 2B6 or 3A4. ³⁵	BCRP (intestinal) ³⁵ , P-gp (in vitro only; not expected to cause clinically significant interactions via P-gp inhibition at usual clinical doses) ³⁸ Does not inhibit OATP1B ³⁵	
ledipasvir ³¹	P-gp (likely)	Not an inhibitor or inducer of P450 or UGT.	Not an inhibitor or inducer of P450 or UGT.	Weak inhibitor of P-gp and BRCP (intestinal, not systemic). Likely a weak inhibitor of OATP1B1/1B3.	
ombitasvir ^{32, 33}	3A4, P-gp, BCRP.	UGT1A1 (net effect of 3D is UGT1A1 inhibition) ³⁴			
velpatasvir (GS-5816) ^{28, 29}	CYP3A4, 2C8, 2B6; OATP1B1, OATP1B3, P-gp, BCRP.	No inhibiting or inducing effects on P450.	No inhibiting or inducing effects on P450.	P-gp (weak), OATP1B1, 1B3, 2B1 (weak), BCRP (moderate).	
HCV NS5B INHIBIT	TORS				
beclabuvir ^{44, 45}	CYP3A4, P-gp; OATP1B1/1B3		CYP3A4 (weak- moderate); 46-50% ↓ midazolam AUC	P-gp	
dasabuvir ^{32, 33}	CYP2C8>3A4, P-gp, BCRP.	UGT1A1 (net effect of 3D is UGT1A1 inhibition) ³⁴		BCRP, P-gp (potential)	
sofosbuvir ³⁰	P-gp, BCRP.GS- 331007 (primary systemic nucleoside	No inhibiting or inducing effects on P450 and UGT1A1.	No inhibiting or inducing effects on P450 and UGT1A1.	No inhibiting or inducing effects on P-gp, BCRP, OATP1B1,	No inhibiting or inducing effects on P-gp, BCRP,

	Substrate	CYP450 and UGT		Transporters	
		Inhibitor	Inducer	Inhibitor	Inducer
	metabolite, accounts for >90% of systemic drug exposure): not a P-gp substrate			OATP1B3, OCT1, BSEP.	OATP1B1, OATP1B3, OCT1, BSEP.
HCV NS3/4A PIs					
asunaprevir 42,43	CYP3A4, P-gp; OATP1B/2B1	CYP2D6 (moderate)	CYP3A4 (weak)	P-gp, OATP1B1/2B1 (weak)	
grazoprevir ^{37, 39}	CYP3A4, P-gp and OATP1B1	CYP2C8 (not clinically meaningful), 40 3A4 (weak), UGT1A1 (weak)	Does not induce CYP1A2, 2B6 or 3A4. ³⁵	BCRP (intestinal) ³⁵ . Does not inhibit OATP1B ³⁵	
paritaprevir ^{32, 33}	3A4, P-gp, OATP1B1, OATP1B3, BCRP.	UGT1A1 (net effect of 3D is UGT1A1 inhibition) ³⁴		OATP1B1 and OATP1B3; P-gp, BCRP (potential).	
simeprevir	CYP3A4, P-gp, OATP1B1.	Mild inhibitor of intestinal (but not hepatic) CYP3A4, and 1A2. ⁴⁷ No clinically relevant effects on CYP2C9, 2C19 and 2D6. ⁴⁸		P-gp, OATP1B1/3	
voxilaprevir (GS- 9857) ⁴¹	CYP3A4, 2C8, P-gp, BCRP, OATPs			P-gp, BCRP, OATPs	

<u>Key</u>: BCRP = breast cancer resistance protein; CYP= Hepatic Cytochrome P450 isoenzyme; Substrate= route of hepatic elimination of that specific drug (specified by a specific cytochrome P450 isoenzyme); inducer = leads to more rapid clearance of substrates of a specific hepatic isoenzyme (lowers serum concentrations of the respective drug and may lead to decreased efficacy); inhibitor= leads to decreased clearance of substrates of a specific hepatic isoenzyme (increases serum concentrations of a respective drug and may lead to toxicity). OCT2 = renal organic cation transporter; P-gp= P-glycoprotein; UGT= Uridine diphosphate glucuronyltransferase.

Please note: This chart summarizes currently available data, and should be used in conjunction with other reliable sources of information. Due to the rapidly changing nature of information about HIV treatment and therapies, users are advised to recheck the information contained herein with the original source before applying it to patient care.

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