Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

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This table provides information on the known or predicted interactions between protease inhibitors (PIs) and non-antiretroviral (ARV) drugs. The term "PI" refers to atazanavir (ATV) or darunavir (DRV) boosted with either ritonavir (RTV or r) or cobicistat (COBI or c). This table does not include interactions for unboosted ATV, fosamprenavir (FPV), lopinavir (LPV), nelfinavir (NFV), or tipranavir (TPV). For information regarding interactions between PIs and other ARV drugs, including dosing recommendations, refer to Tables 24c, 25a, and 25b.

Recommendations for managing particular drug interactions may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgment to select the most appropriate alternative medication.

Note: Unboosted ATV, FPV, LPV/r, NFV, and TPV are no longer commonly used in clinical practice in the United States and are **not** included in this table. Please refer to the U.S. Food and Drug Administration product labels for information regarding drug interactions between these PIs and concomitant medications. Information regarding these agents may also be found in archived versions of this guideline.

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Antacids	ATV/c, ATV/r	**When Given Simultaneously** • ↓ ATV expected	Administer ATV at least 2 hours before or 2 hours after antacids or buffered medications.
H2 Receptor Antagonists	ATV/c, ATV/r	↓ ATV expected	H2RA dose should not exceed a dose equivalent to famotidine 40 mg twice daily in ART-naive patients or famotidine 20 mg twice daily in ART-experienced patients. Give ATV 300 mg (plus COBI 150 mg **or** RTV 100 mg) with food simultaneously with and/or ≥10 hours after the dose of H2RA.

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			If using TDF and H2RA in ART-experienced patients, administer ATV 400 mg plus RTV 100 mg with food simultaneously with and/or ≥10 hours after the dose of H2RA. **Do not coadminister** ATV/c with TDF and H2RA in ART-experienced patients.
	DRV/c, DRV/r	**With Ranitidine** • ↔ DRV/r	No dose adjustment needed
Proton Pump Inhibitors	ATV/c, ATV/r	**With Omeprazole 40 mg** • ATV AUC ↓ 76% **When Omeprazole 20 mg Is Given 12 Hours Before ATV/c or ATV/r** • ATV AUC ↓ 42%	PPI dose should not exceed a dose equivalent to omeprazole 20 mg daily in PI-naive patients. PPIs should be administered at least 12 hours before ATV/c or ATV/r. **Do not coadminister** in PI-experienced patients.
	DRV/c	↔ PI expected	No dose adjustment needed
	DRV/r	↔ DRV/r Omeprazole AUC ↓ 42%	Consider alternative ARV or acid reducer. If coadministered, monitor for omeprazole effectiveness. If the patient does not experience symptomatic relief, increase the dose to no more than omeprazole 40 mg daily.
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia			
Alfuzosin	ATV/c, ATV/r, DRV/c, DRV/r	↑ alfuzosin expected	**Contraindicated**
Doxazosin	ATV/c, ATV/r, DRV/c, DRV/r	↑ doxazosin possible	Initiate doxazosin at lowest dose and titrate. Monitor blood pressure. Dose reduction may be necessary.

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Tamsulosin	ATV/c, ATV/r, DRV/c, DRV/r	↑ tamsulosin expected	**Do not coadminister** unless benefits outweigh risks**.** If coadministered, monitor blood pressure.
Terazosin	ATV/c, ATV/r, DRV/c, DRV/r	↔ or ↑ terazosin possible	Initiate terazosin at lowest dose and titrate. Monitor blood pressure. Dose reduction may be necessary.
Silodosin	ATV/c, ATV/r, DRV/c, DRV/r	↑ silodosin expected	**Contraindicated**
Antibacterials—Antimycobacterials			
Bedaquiline	ATV/c, ATV/r, DRV/c, DRV/r	• ↑ bedaquiline possible	**Do not coadminister** unless benefits outweigh risks. If coadministered, consider therapeutic drug monitoring and monitor for bedaquiline-related adverse effects, including hepatotoxicity and QTc prolongation.
Rifabutin	ATV/r	**Compared With Rifabutin (300 mg Once Daily) Alone, Rifabutin (150 mg Once Daily) Plus ATV/r** • Rifabutin AUC ↑ 110% and metabolite AUC ↑ 2,101%	Recommended dose is rifabutin 150 mg once daily. Monitor for antimycobacterial activity and consider therapeutic drug monitoring. Monitor for rifabutin-related adverse events, including neutropenia and uveitis. PK data in this table are results from healthy volunteer studies. Lower rifabutin exposure has been reported in patients with HIV than in healthy study participants.
	DRV/r	**Compared With Rifabutin (300 mg Once Daily) Alone, Rifabutin (150 mg Every Other Day) Plus DRV/r** • ↔ rifabutin AUC and metabolite AUC ↑ 881%	
	ATV/c, DRV/c	↑ rifabutin expected ↓ COBI expected	**Do not coadminister.**

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Rifampin	ATV/c, ATV/r, DRV/c, DRV/r	↓ PI concentration by >75%	**Contraindicated.** Increasing the dose of RTV does not overcome this interaction and may increase hepatotoxicity. Increasing the COBI dose **is not recommended.** Consider rifabutin if a rifamycin is indicated.
Rifapentine	ATV/c, ATV/r, DRV/c, DRV/r	**Daily and Weekly Dosing** • ↓ PI expected	**Do not coadminister.**
Antibacterials—Macrolides			
Azithromycin	ATV/c, ATV/r	↑ azithromycin possible	No dose adjustment needed
	DRV/c, DRV/r	↔ azithromycin expected	No dose adjustment needed
Clarithromycin	ATV/c, ATV/r, DRV/c	↑ clarithromycin expected ↑ ATV/r and PI/c expected	Consider alternative ARV or azithromycin.
	DRV/r	DRV/r ↑ clarithromycin AUC 57% RTV 500 mg twice daily ↑ clarithromycin 77%	Consider alternative ARV or azithromycin. If use of clarithromycin is necessary in a patient with impaired renal function, reduce clarithromycin dose by 50% in patients with CrCl 30 to 60 mL/min. In patients with CrCl <30 mL/min, reduce clarithromycin dose by 75%. Monitor for clarithromycin-related adverse events, including QTc prolongation.
Erythromycin	ATV/c, ATV/r, DRV/c, DRV/r	↑ erythromycin expected ↑ PI expected	Consider alternative ARV or use azithromycin.

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Anticoagulants			
Apixaban	ATV/c, ATV/r, DRV/c, DRV/r	↑ apixaban expected	**Do not coadminister** in patients who require apixaban 2.5 mg twice daily. **In Patients Requiring Apixaban 5 mg or 10 mg Twice Daily** • Reduce apixaban dose by 50%.
Dabigatran	ATV/c, ATV/r	**With COBI 150 mg Alone** • Dabigatran AUC ↑ 110% to 127% **With ATV/r** • ↑ dabigatran expected	**Reduction of Risk of Stroke and Systemic Embolism in Nonvalvular Atrial Fibrillation in Adult Patients** • CrCl >30 mL/min: no dose adjustment needed • CrCl ≤30 mL/min: do not coadminister. **Treatment and Reduction in the Risk of Recurrence of DVT and PE or Prophylaxis of DVT and PE Following Hip Replacement Surgery in Adult Patients** • CrCl ≥50 mL/min: no dose adjustment needed • CrCl <50 mL/min: do not coadminister.
	DRV/c, DRV/r	**With DRV/c** • Single dose DRV/c: dabigatran AUC ↑ 164% • After 14 days of DRV/c: dabigatran AUC ↑ 88% **With DRV/r** • Single dose DRV/r: dabigatran AUC ↑ 72% • After 14 days of daily DRV/r: dabigatran AUC ↑ 18%	
Edoxaban	ATV/c, ATV/r, DRV/c	↑ edoxaban expected	**Treatment of Nonvalvular Atrial Fibrillation** • No dose adjustment needed **Treatment of DVT and PE** • Reduce edoxaban dose to 30 mg once daily.

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	DRV/r	↑ edoxaban expected	**Treatment of Nonvalvular Atrial Fibrillation** • No dose adjustment needed **Treatment of DVT and PE** • No dose adjustment needed
Rivaroxaban	ATV/c, ATV/r, DRV/c, DRV/r	↑ rivaroxaban expected	**Do not coadminister.**
Warfarin	ATV/c, DRV/c	↑ warfarin possible	Monitor INR closely when stopping or starting PI/c or PI/r and adjust warfarin dose accordingly. If switching between RTV and COBI, the effect of COBI on warfarin is not expected to be equivalent to RTV's effect on warfarin.
	ATV/r, DRV/r	↓ warfarin possible	
Antidepressants, Anxiolytics, and Antipsychotics Also see the Sedative/Hypnotics section below			
Antidepressants, Anxiolytics			
Bupropion	ATV/r, DRV/r	↓ bupropion possible	Titrate bupropion dose based on clinical response.
	ATV/c, DRV/c	↔ bupropion expected	No dose adjustment needed
Buspirone	ATV/c, ATV/r, DRV/c, DRV/r	↑ buspirone expected	Administer lowest dose of buspirone with caution and titrate buspirone dose based on clinical response. Dose reduction may be necessary. Monitor for buspirone-related adverse events.
Desvenlafaxine	ATV/c, ATV/r, DRV/c, DRV/r	↑ desvenlafaxine possible	No dose adjustment needed

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Duloxetine	ATV/c, DRV/c	↑ duloxetine possible	No dose adjustment needed
	ATV/r, DRV/r	↑ or ↓ duloxetine possible	
Mirtazapine	ATV/c, ATV/r, DRV/c, DRV/r	↑ mirtazapine possible	Monitor for mirtazapine-related adverse events. Mirtazapine dose reduction may be necessary.
Nefazodone	ATV/c, ATV/r, DRV/c, DRV/r	↑ nefazodone expected ↑ PI possible	Monitor for nefazodone-related adverse events and PI tolerability.
Selective Serotonin Reuptake Inhibitors (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, vortioxetine)	DRV/r	Paroxetine AUC ↓ 39% Sertraline AUC ↓ 49%	Titrate SSRI dose based on clinical response.
	ATV/c, ATV/r, DRV/c	↑ or ↓ SSRI possible	Titrate SSRI dose using the lowest available initial or maintenance dose.
Trazodone	ATV/c, ATV/r, DRV/c, DRV/r	**RTV 200 mg Twice Daily (For 2 Days)** • Trazodone ↑ AUC 240%	Administer lowest dose of trazodone and titrate dose based on clinical response. Monitor for trazodone-related adverse events, including CNS and CV adverse events.
Tricyclic Antidepressants (e.g., amitriptyline, doxepin, nortriptyline)	ATV/c, ATV/r, DRV/c, DRV/r	↑ TCA expected	Administer lowest possible TCA dose and titrate based on clinical assessment and/or drug concentrations. Monitor for TCA-related adverse events.
Venlafaxine	ATV/c, ATV/r, DRV/c, DRV/r	↑ venlafaxine and O-desmethylvenlafaxine expected	Monitor for venlafaxine-related adverse events. Consider venlafaxine dose reduction.

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Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antipsychotics			
Aripiprazole	ATV/c, ATV/r, DRV/c, DRV/r	↑ aripiprazole expected	Administer 25% of the usual aripiprazole dose. Titrate dose based on clinical monitoring for effectiveness/adverse events. Refer to aripiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6-poor metabolizers.
Brexpiprazole	ATV/c, ATV/r, DRV/c, DRV/r	↑ brexpiprazole expected	Administer 25% of the usual brexpiprazole dose. Titrate the dose based on clinical monitoring for effectiveness/adverse events. Refer to brexpiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6-poor metabolizers.
Cariprazine	ATV/c, ATV/r, DRV/c, DRV/r	↑ cariprazine expected	**Starting Cariprazine in a Patient Who Is Already Receiving a PI** • Administer cariprazine 1.5 mg on Day 1 and Day 3, with no dose given on Day 2. From Day 4 onward, administer cariprazine 1.5 mg daily. Dose can be increased to a maximum of cariprazine 3 mg daily. If the PI is withdrawn, cariprazine dose may need to be increased. **Starting a PI in a Patient Who Is Already Receiving Cariprazine** • For patients receiving cariprazine 3 mg or cariprazine 6 mg daily, reduce the dose by half. For patients taking cariprazine 4.5 mg daily, the dose should be reduced to cariprazine 1.5 mg or cariprazine 3 mg daily. For patients taking cariprazine 1.5 mg daily, change to cariprazine 1.5 mg every other day. If PI is withdrawn, the cariprazine dose may need to be increased.

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Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Iloperidone	ATV/c, ATV/r, DRV/c, DRV/r	↑ iloperidone expected	Decrease iloperidone dose by 50%.
Lumateperone	ATV/c, ATV/r, DRV/c, DRV/r	↑ lumateperone expected	**Do not coadminister.**
Lurasidone	ATV/c, ATV/r, DRV/c, DRV/r	↑ lurasidone expected	**Contraindicated**
Olanzapine, Olanzapine/Samidorphan	ATV/c, DRV/c	↔ olanzapine expected ↑ samidorphan possible	No dose adjustment needed
	ATV/r, DRV/r	↓ olanzapine possible	Monitor for therapeutic effectiveness of olanzapine.
Other Antipsychotics **CYP3A4 and/or CYP2D6 substrates** (e.g., clozapine, perphenazine, risperidone, thioridazine)	ATV/c, ATV/r, DRV/c, DRV/r	↑ antipsychotic possible	Titrate the antipsychotic dose using the lowest initial dose or adjust the maintenance dose accordingly. Monitor for adverse events, including QTc prolongation.
Pimavanserin	ATV/c, ATV/r, DRV/c, DRV/r	↑ pimavanserin expected	Reduce pimavanserin dose to 10 mg once daily.
Pimozide	ATV/c, ATV/r, DRV/c, DRV/r	↑ pimozide expected	**Contraindicated**
Quetiapine	ATV/c, ATV/r, DRV/c, DRV/r	↑ quetiapine expected	**Starting Quetiapine in a Patient Receiving a PI** • Initiate quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine effectiveness and adverse events, including QTc prolongation.

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Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
			Starting a PI in a Patient Receiving a Stable Dose of Quetiapine • Consider alternative ARV. If coadministered, reduce quetiapine dose to 1/6 of the current dose. Closely monitor for quetiapine effectiveness and adverse events, including QTc prolongation.
Ziprasidone	ATV/c, ATV/r, DRV/c, DRV/r	↑ ziprasidone expected	Monitor for ziprasidone-related adverse events, including QTc prolongation.
Antifungals			
Fluconazole	ATV/c, ATV/r, DRV/c, DRV/r	↔ PI expected ↔ fluconazole expected	No dose adjustment needed
Isavuconazole	ATV/c, DRV/c	↑ isavuconazole expected ↓ PI possible	**Contraindicated**
	ATV/r, DRV/r	↑ isavuconazole expected ↓ PI possible	If coadministered, monitor isavuconazole concentrations and monitor for isavuconazole-related adverse events. Monitor for PI tolerability.
Ibrexafungerp	ATV/c, ATV/r, DRV/c, DRV/r	↑ ibrexafungerp expected	Reduce ibrexafungerp dose to 150 mg twice daily.
Itraconazole	ATV/c, ATV/r, DRV/c, DRV/r	↑ itraconazole expected ↑ PI expected	Itraconazole doses >200 mg/day **are not recommended** unless dosing is guided by itraconazole concentrations.
Posaconazole	ATV/r	ATV AUC ↑ 146% ↔ posaconazole possible	If coadministered, monitor for PI-related adverse events.
	ATV/c, DRV/c, DRV/r	↑ PI expected ↔ posaconazole possible	

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Voriconazole	ATV/c, DRV/c	No data	**Do not coadminister** voriconazole and RTV or COBI unless benefits outweigh risks. If coadministered, monitor voriconazole concentration and adjust dose accordingly.
	ATV/r, DRV/r	RTV 100 mg twice daily ↓ voriconazole AUC 39%	
Antimalarials			
Artemether/Lumefantrine	ATV/c, DRV/c	↑ lumefantrine expected ↑ artemether possible	Clinical significance is unknown. If coadministered, monitor closely for antimalarial effectiveness and lumefantrine-related adverse events, including QTc prolongation.
	DRV/r	↔ artemether expected ↔ DHA[a] expected Lumefantrine AUC ↑ 175% ↔ DRV	
Artesunate	ATV/c	↑ DHA[a] possible	Monitor for artesunate-related adverse effects.
	DRV/c	↔ DHA[a] expected	No dose adjustment needed
	ATV/r, DRV/r	↓ DHA[a] possible	Monitor for clinical response to artesunate.
Atovaquone/Proguanil	ATV/r, DRV/r	**With ATV/r** • Atovaquone AUC ↓ 46% • Proguanil AUC ↓ 41% **With DRV/r** • ↓ atovaquone/proguanil possible	Clinical significance is unknown. Consider alternative ARV or malaria prophylaxis.
	ATV/c, DRV/c	↔ atovaquone/proguanil expected	No dose adjustment needed

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Mefloquine	ATV/c, ATV/r, DRV/c, DRV/r	**With RTV 200 mg Twice Daily** • RTV AUC ↓ 31% and C_{min} ↓ 43% • ↔ mefloquine **With ATV (Unboosted), PI/c, or PI/r** • ↑ mefloquine possible	Clinical significance is unknown. Consider alternative ARV or antimalarial drug. If coadministered, monitor for mefloquine-related adverse events, including psychiatric symptoms and QTc prolongation. Monitor virologic response.
Antimigraine			
Ergot Derivatives	ATV/c, ATV/r, DRV/c, DRV/r	↑ dihydroergotamine, ergotamine, and methylergonovine expected	**Contraindicated**
Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists			
Atogepant	ATV/c, ATV/r, DRV/c, DRV/r	↑ atogepant expected	Chronic migraine: **Do not coadminister.** Episodic migraine: Administer atogepant at a dose of 10 mg once daily.
Rimegepant	ATV/c, ATV/r, DRV/c, DRV/r	↑ rimegepant expected	**Do not coadminister.**
Ubrogepant	ATV/c, ATV/r, DRV/c, DRV/r	↑ ubrogepant expected	**Contraindicated**
Zavegepant	ATV/r, ATV/c, DRV/c	↑ zavegepant expected	**Do not coadminister.**
	DRV/r	↔ zavegepant expected	No dose adjustment needed

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Serotonin 5-HT1B, 1D Receptor Agonists			
Almotriptan	ATV/c, ATV/r, DRV/c, DRV/r	↑ almotriptan expected	Administer single dose of almotriptan 6.25 mg. Maximum dose should not exceed 12.5 mg in a 24-hour period.
Eletriptan	ATV/c, ATV/r, DRV/c, DRV/r	↑ eletriptan expected	**Contraindicated**
Frovatriptan, Naratriptan, Rizatriptan, Sumatriptan, Zolmitriptan	ATV/c, ATV/r, DRV/c, DRV/r	↔ triptan expected	No dose adjustment needed
Antiplatelets			
Clopidogrel	ATV/c, ATV/r, DRV/c, DRV/r	Clopidogrel active metabolite AUC ↓ 69% in people with HIV on RTV or COBI-boosted regimens compared with healthy volunteers without HIV. Impaired platelet inhibition observed in people with HIV.	**Do not coadminister.**
Prasugrel	ATV/c, ATV/r, DRV/c, DRV/r	Prasugrel active metabolite AUC ↓ 52% in people with HIV on RTV or COBI-boosted regimens compared to healthy volunteers without HIV. Adequate platelet inhibition observed in people with HIV.	No dose adjustment needed
Ticagrelor	ATV/c, ATV/r, DRV/c, DRV/r	↑ ticagrelor expected	**Do not coadminister.**
Vorapaxar	ATV/c, ATV/r, DRV/c, DRV/r	↑ vorapaxar expected	**Do not coadminister.**

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Antipneumocystis and Antitoxoplasmosis			
Atovaquone Oral suspension	ATV/r	↔ atovaquone	No dose adjustment needed
	ATV/c, DRV/c, DRV/r	↔ atovaquone expected	No dose adjustment needed
Antiseizure			
Carbamazepine	ATV/r	↑ carbamazepine possible May ↓ PI concentrations substantially	Consider alternative ARV or anticonvulsant. If coadministration is necessary, consider monitoring concentrations of both drugs and assess virologic response. Carbamazepine dose reduction may be necessary.
	DRV/r	Carbamazepine AUC ↑ 45% ↔ DRV	Monitor anticonvulsant concentration and adjust dose accordingly.
	ATV/c, DRV/c	↑ carbamazepine possible ↓ COBI expected ↓ PI expected	**Contraindicated**
Eslicarbazepine	ATV/c, ATV/r, DRV/c, DRV/r	↓ PI possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor for virologic response. Consider monitoring anticonvulsant and PI concentrations.
Ethosuximide	ATV/c, ATV/r, DRV/c, DRV/r	↑ ethosuximide possible	Monitor for ethosuximide-related adverse events.

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Lamotrigine	ATV/r	Lamotrigine AUC ↓ 32%	A dose increase of lamotrigine may be needed; monitor lamotrigine concentration or consider alternative ARV or anticonvulsant.
	DRV/r	↓ lamotrigine possible	
	ATV/c	No data	Monitor anticonvulsant concentration and adjust dose accordingly.
	DRV/c	↔ lamotrigine expected	No dose adjustment needed.
Oxcarbazepine	ATV/c, ATV/r, DRV/c, DRV/r	↓ PI possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor for virologic response. Consider monitoring anticonvulsant and PI concentrations.
Phenobarbital	ATV/r, DRV/r	↓ phenobarbital possible ↓ PI possible	Consider alternative anticonvulsant. If coadministration is necessary, consider monitoring concentrations of both drugs and assessing virologic response.
	ATV/c, DRV/c	↓ COBI expected ↓ PI expected	**Contraindicated**
Phenytoin	ATV/r, DRV/r	↓ phenytoin possible ↓ PI possible	Consider alternative anticonvulsant. If coadministration is necessary, consider monitoring concentrations of both drugs and assessing virologic response.
	ATV/c, DRV/c	↓ COBI expected ↓ PI expected	**Contraindicated**
Primidone	ATV/c, ATV/r, DRV/c, DRV/r	↓ PI expected	**Do not coadminister.**
Valproic Acid	ATV/c, ATV/r, DRV/c, DRV/r	↓ or ↔ VPA possible	Monitor VPA concentrations and monitor for PI tolerability.

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Antivirals—Hepatitis C			
Elbasvir/Grazoprevir	ATV/r	Elbasvir AUC ↑ 4.8-fold Grazoprevir AUC ↑ 10.6-fold Elbasvir ↔ ATV Grazoprevir ↑ ATV AUC 43%	**Contraindicated** May increase the risk of ALT elevations due to a significant increase in grazoprevir plasma concentrations caused by OATP1B1/3 inhibition.
	DRV/r	Elbasvir AUC ↑ 66% Grazoprevir AUC ↑ 7.5-fold ↔ DRV	
	ATV/c, DRV/c	↑ grazoprevir expected	
Glecaprevir/Pibrentasvir	ATV/c, ATV/r	**With (ATV 300 mg Plus RTV 100 mg) Once Daily** • Glecaprevir AUC ↑ 6.5-fold • Pibrentasvir AUC ↑ 64%	**Contraindicated**
	DRV/c, DRV/r	**With (DRV 800 mg Plus RTV 100 mg) Once Daily** • Glecaprevir AUC ↑ fivefold • ↔ pibrentasvir	**Do not coadminister.**
Ledipasvir/Sofosbuvir	ATV/r	ATV AUC ↑ 33% Ledipasvir AUC ↑ 113% ↔ sofosbuvir	No dose adjustment needed Coadministration of ledipasvir/sofosbuvir with TDF and a PI/r results in increased exposure to TDF. The safety of the increased TDF exposure has not been established. Consider alternative HCV or ARV drugs to avoid increased risk of TDF toxicities. If coadministration is necessary, monitor for TDF-related adverse events.
	ATV/c, DRV/c, DRV/r	↔ PI expected ↔ ledipasvir and sofosbuvir	

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Sofosbuvir/Velpatasvir	ATV/r	↔ ATV/r ↔ sofosbuvir Velpatasvir AUC ↑ 2.4-fold	No dose adjustment needed
	DRV/r	↔ DRV/r Sofosbuvir AUC ↓ 28% ↔ velpatasvir	No dose adjustment needed
	ATV/c, DRV/c	↔ sofosbuvir and velpatasvir expected	No dose adjustment needed
Sofosbuvir/Velpatasvir/ Voxilaprevir	ATV/c, ATV/r	**With ATV/r** • Voxilaprevir AUC ↑ 4.3-fold • Velpatasvir AUC ↑ 93% • Sofosbuvir AUC ↑ 40%	**Do not coadminister.**
	DRV/c, DRV/r	**With DRV/r** • Voxilaprevir AUC ↑ 2.4-fold • ↔ DRV/r, velpatasvir, and sofosbuvir	No dose adjustment needed
Antivirals—Miscellaneous (e.g., for CMV, Mpox)			
Brincidofovir	ATV/c, ATV/r, DRV/c, DRV/r	↑ brincidofovir possible	Give PI dose at least 3 hours after administering brincidofovir and monitor for brincidofovir-related adverse events (i.e., elevations in ALT/AST and bilirubin and GI adverse events).
Cidofovir	ATV/c, ATV/r, DRV/c, DRV/r	↔ cidofovir	No dose adjustment needed

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Tecovirimat	ATV/c, ATV/r, DRV/c, DRV/r	↔ tecovirimat	No dose adjustment needed
Antivirals—SARS-CoV-2			
Molnupiravir	ATV/c, ATV/r, DRV/c, DRV/r	↔ molnupiravir	No dose adjustment needed
Remdesivir	ATV/c, ATV/r, DRV/c, DRV/r	↔ remdesivir	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	ATV/r, ATV/c, DRV/c, DRV/r	↑ PI expected ↑ ritonavir-boosted nirmatrelvir expected	No dose adjustment needed. Monitor for increased ritonavir-boosted nirmatrelvir and PI-related adverse events.
Beta-Agonists, Long-Acting Inhaled			
Arformoterol, Formoterol	ATV/c, ATV/r	↑ arformoterol possible	No dose adjustment needed
	DRV/c, DRV/r	↔ arformoterol expected	No dose adjustment needed
Indacaterol	ATV/c, ATV/r, DRV/c, DRV/r	**With RTV 300 mg Twice Daily** • Indacaterol AUC ↑ 1.7-fold	No dose adjustment needed in patients receiving indacaterol 75 mcg daily.
Olodaterol	ATV/c, ATV/r, DRV/c, DRV/r	↑ olodaterol expected	No dose adjustment needed
Salmeterol	ATV/c, ATV/r, DRV/c, DRV/r	↑ salmeterol possible	**Do not coadminister,** due to potential increased risk of salmeterol-related CV events.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cardiac Medications			
Antiarrhythmics			
Amiodarone	ATV/r	↑ amiodarone possible ↑ PI possible	**Contraindicated**
	ATV/c, DRV/c, DRV/r	↑ amiodarone possible ↑ PI possible	**Do not coadminister** unless the benefits outweigh the risks. If coadministered, monitor for amiodarone-related adverse events and consider monitoring ECG and amiodarone drug concentration.
Digoxin	ATV/c, ATV/r, DRV/c, DRV/r	RTV 200 mg twice daily ↑ digoxin AUC 29% and ↑ half-life 43% DRV/r ↑ digoxin AUC 36% COBI ↑ digoxin C_{max} 41% and ↔ AUC	Monitor digoxin concentrations. Digoxin dose may need to be decreased. Titrate initial digoxin dose.
Disopyramide	ATV/c, ATV/r, DRV/c, DRV/r	↑ disopyramide possible	**Do not coadminister.**
Dofetilide	ATV/c, ATV/r, DRV/c, DRV/r	↑ dofetilide possible	**Do not coadminister.**
Dronedarone	ATV/c, ATV/r, DRV/c, DRV/r	↑ dronedarone expected	**Contraindicated**
Flecainide	ATV/c, ATV/r, DRV/c, DRV/r	↑ flecainide possible	Consider alternative ARV or antiarrhythmic. If coadministered, monitor flecainide concentrations and for antiarrhythmic-related adverse events.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lidocaine	ATV/c, ATV/r, DRV/c, DRV/r	↑ lidocaine possible	Consider alternative ARV or antiarrhythmic. If coadministered, monitor lidocaine concentrations and for antiarrhythmic-related adverse events.
Mexiletine	ATV/c, ATV/r, DRV/c, DRV/r	↑ mexiletine possible	Consider alternative ARV or antiarrhythmic. If coadministered, monitor mexiletine concentrations and for antiarrhythmic-related adverse events.
Propafenone	ATV/c, ATV/r, DRV/c, DRV/r	↑ propafenone possible	**Do not coadminister.**
Quinidine	ATV/r	↑ quinidine expected	**Contraindicated**
	ATV/c, DRV/c, DRV/r	↑ quinidine possible	**Do not coadminister.**
Sotalol	ATV/c, ATV/r, DRV/c, DRV/r	↔ sotalol expected	No dose adjustment needed
Beta-Blockers			
Atenolol, Labetalol	ATV/c, ATV/r, DRV/c, DRV/r	↑ beta-blockers possible	No dose adjustment needed
Bisoprolol, Carvedilol, Metoprolol, Nebivolol	ATV/c, ATV/r, DRV/c, DRV/r	↑ beta-blockers possible	May need to decrease beta-blocker dose; adjust dose based on clinical response. Consider using beta-blockers that are not metabolized by CYP2D6 enzymes (e.g., atenolol, labetalol, nadolol).
Calcium Channel Blockers			
Amlodipine, Diltiazem, Felodipine, Nifedipine, Verapamil	ATV/c, ATV/r, DRV/c, DRV/r	↑ dihydropyridine possible ↑ verapamil possible	Titrate CCB dose and monitor closely. ECG monitoring is recommended when CCB is used with ATV.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Diltiazem	ATV/c, ATV/r	Unboosted ATV ↑ diltiazem AUC 125% Greater ↑ of diltiazem AUC is likely with ATV/c or ATV/r	Decrease diltiazem dose by at least 50%. If starting diltiazem, start with the lowest dose and titrate according to clinical response and adverse events. ECG monitoring is recommended.
	DRV/c, DRV/r	↑ diltiazem possible	Titrate diltiazem dose according to clinical response and adverse events.
Cardiac—Other			
Bosentan	ATV/c, ATV/r, DRV/c, DRV/r	**With ATV (Unboosted)** • ↓ ATV expected **With PI/r or PI/c** • ↑ bosentan expected	**Do not coadminister** bosentan and unboosted ATV. **In Patients on a PI (Other Than Unboosted ATV) >10 Days** • Start bosentan at 62.5 mg once daily or every other day. **In Patients on Bosentan Who Require a PI (Other Than Unboosted ATV)** • Stop bosentan ≥36 hours before PI initiation and restart bosentan 10 days after PI initiation at 62.5 mg once daily or every other day. **When Switching Between COBI and RTV** • Maintain same bosentan dose.
Eplerenone	ATV/c, ATV/r, DRV/c, DRV/r	↑ eplerenone expected	**Contraindicated**
Ivabradine	ATV/c, ATV/r, DRV/c, DRV/r	↑ ivabradine expected	**Contraindicated**
Mavacamten	ATV/c, ATV/r, DRV/c, DRV/r	↑ mavacamten expected	**Contraindicated**

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Ranolazine	ATV/c, ATV/r, DRV/c, DRV/r	↑ ranolazine expected	**Contraindicated**
Corticosteroids			
Beclomethasone Inhaled or intranasal	DRV/r	↔ 17-BMP (active metabolite) AUC RTV 100 mg twice daily ↑ 17-BMP AUC 2-fold	No dose adjustment needed
	ATV/c, ATV/r, DRV/c	↔ 17-BMP expected	No dose adjustment needed
Budesonide, Ciclesonide, Fluticasone, Mometasone Inhaled or intranasal	ATV/c, ATV/r, DRV/c, DRV/r	↑ glucocorticoids possible RTV 100 mg twice daily ↑ fluticasone AUC 350-fold	**Do not coadminister** unless the potential benefits of inhaled or intranasal corticosteroid outweigh the risks of adverse events associated with corticosteroids. Coadministration can result in adrenal insufficiency and Cushing's syndrome. Consider alternative inhaled/intranasal corticosteroid (e.g., beclomethasone).
Betamethasone, Budesonide Systemic	ATV/c, ATV/r, DRV/c, DRV/r	↑ glucocorticoids possible ↓ PI possible	**Do not coadminister** unless the potential benefits of systemic corticosteroid outweigh the risks of adverse events associated with systemic corticosteroids. Coadministration can result in adrenal insufficiency and Cushing's syndrome.
Dexamethasone Systemic	ATV/c, ATV/r, DRV/c, DRV/r	↑ glucocorticoids possible ↓ PI possible	Consider alternative corticosteroid for long-term use. If coadministration is necessary, monitor virologic response to ART.
Prednisone, Prednisolone Systemic	ATV/c, ATV/r, DRV/c, DRV/r	↑ prednisolone possible	Coadministration may be considered if the potential benefits outweigh the risks of adverse events associated with systemic corticosteroids. If coadministered, monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-related adverse events.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Betamethasone, Methylprednisolone, Triamcinolone Local injections, including intra-articular, epidural, or intra-orbital	ATV/c, ATV/r, DRV/c, DRV/r	↑ glucocorticoids expected	**Do not coadminister.** Coadministration can result in adrenal insufficiency and Cushing's syndrome.
Glucose-Lowering			
Canagliflozin	ATV/c, DRV/c	↔ canagliflozin	No dose adjustment needed
	ATV/r, DRV/r	↓ canagliflozin expected	If a patient is already tolerating canagliflozin 100 mg daily, increase canagliflozin dose to 200 mg daily. If a patient is already tolerating canagliflozin 200 mg daily and requires additional glycemic control, management strategy is based on renal function. **In Patients With eGFR ≥60 mL/min/1.73 m^2** • Canagliflozin dose may be increased to 300 mg daily. **In Patients With eGFR <60 mL/min/1.73 m^2** • Consider adding another antihyperglycemic agent.
Saxagliptin	ATV/c, ATV/r, DRV/c, DRV/r	↑ saxagliptin expected	Limit saxagliptin dose to 2.5 mg once daily.
Dapagliflozin/Saxagliptin	ATV/c, ATV/r, DRV/c, DRV/r	↑ saxagliptin expected	**Do not coadminister.** Dapagliflozin is only available as a coformulated drug that contains 5 mg of saxagliptin. When coadministered with EVG/c, the dose of saxagliptin should not exceed 2.5 mg once daily; thus, this combination **is not recommended.**

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Herbal Products			
St. John's Wort	ATV/c, ATV/r, DRV/c, DRV/r	↓ PI expected	**Contraindicated**
Hormonal Therapies—Contraceptives			
Injectable Contraceptives Depot MPA	ATV/c, ATV/r, DRV/c, DRV/r	↔ expected	No dose adjustment needed
Oral Contraceptives (e.g., desogestrel, drospirenone, ethinyl estradiol, levonorgestrel, norgestimate, norethindrone)	ATV/c	Drospirenone AUC ↑ 130% Ethinyl estradiol AUC ↓ 22%	**Contraindicated** with drospirenone-containing hormonal contraceptive due to potential for hyperkalemia. Use alternative ARV or alternative contraceptive methods.
		↔ ethinyl estradiol AUC and C_{min} ↓ 25% ↔ levonorgestrel	No dose adjustment needed
	ATV/r	Ethinyl estradiol AUC ↓ 19% and C_{min} ↓ 37% Norgestimate AUC ↑ 85% Norethindrone AUC ↑ 51% and C_{min} ↑ 67%	Oral contraceptive should contain at least 35 mcg of ethinyl estradiol.[c]
		↑ drospirenone expected ↔ estetrol	Clinical monitoring is recommended due to the potential for hyperkalemia. Use alternative ARV or contraceptive methods.
	DRV/c	Drospirenone AUC ↑ 58% Ethinyl estradiol AUC ↓ 30%	Clinical monitoring is recommended due to the potential for hyperkalemia. Use alternative ARV or contraceptive methods.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	DRV/r	Ethinyl estradiol AUC ↓ 44% and C_{min} ↓ 62% Norethindrone AUC ↓ 14% and C_{min} ↓ 30%	**When Used for Contraception** • Consider alternative ARV or contraceptive methods. If combined, consider using an oral contraceptive with at least 35 mcg of ethinyl estradiol. **When Used for Other Clinical Indications (e.g., Acne, Menstrual Cycle Regulation)** • Monitor for clinical effectiveness of hormonal therapy.
Subdermal Implant Contraceptives (e.g., etonogestrel, levonorgestrel)	ATV/c, ATV/r, DRV/c, DRV/r	↑ etonogestrel, levonorgestrel expected	No dose adjustment needed
Transdermal Contraceptives (e.g., ethinyl estradiol/norelgestromin, ethinyl estradiol/levonorgestrel)	ATV/c, ATV/r, DRV/c, DRV/r	↓ ethinyl estradiol possible with ritonavir ↑ ethinyl estradiol possible with cobicistat ↑ norelgestromin, levonorgestrel possible	No dose adjustment needed
Vaginal Ring Contraceptives (e.g., etonogestrel/ethinyl estradiol, segesterone/ethinyl estradiol)	ATV/r	Ethinyl estradiol AUC ↓ 26% Etonogestrel AUC ↑ 79%	No dose adjustment needed with etonogestrel/ethinyl estradiol vaginal rings. Use alternative ARV or contraceptive methods with segesterone/ethinyl estradiol vaginal rings.
	ATV/c, DRV/c, DRV/r	↓ ethinyl estradiol possible with ritonavir ↑ ethinyl estradiol possible with cobicistat	
Emergency Contraceptives Levonorgestrel (oral)	ATV/c, ATV/r, DRV/c, DRV/r	↑ levonorgestrel expected	No dose adjustment needed

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hormonal Therapies—Miscellaneous			
5-Alpha Reductase Inhibitors (e.g., dutasteride, finasteride)	ATV/c, ATV/r, DRV/c, DRV/r	↑ dutasteride possible ↑ finasteride possible	Adjust dutasteride dose as needed based on clinical effects. No dose adjustment needed for finasteride.
Estradiol	ATV/c, DRV/c	↓ or ↑ estradiol possible	Adjust estradiol dose as needed based on clinical effects.
	ATV/r, DRV/r	↓ estradiol possible	
Goserelin, Leuprolide Acetate, Spironolactone	ATV/c, ATV/r, DRV/c, DRV/r	↔ goserelin, leuprolide acetate, and spironolactone expected	No dose adjustment needed
Menopausal Hormone Replacement Therapy (e.g., conjugated estrogens, drospirenone, estradiol, MPA, progesterone)	ATV/c, ATV/r, DRV/c, DRV/r	↓ or ↑ estrogen possible with estradiol or conjugated estrogen (equine and synthetic)	Adjust estrogen dose as needed based on clinical effects.
	ATV/c, ATV/r, DRV/c, DRV/r	↑ drospirenone possible ↑ MPA ↑ micronized progesterone See the Hormonal Therapies—Contraceptives section for other progestin-PI interactions.	Adjust progestin/progesterone dose as needed based on clinical effects. Drospirenone is not contraindicated with ATV/c products because it is prescribed at a lower dose for menopausal HRT than products used for hormonal contraceptives.
Testosterone	ATV/c, ATV/r, DRV/c, DRV/r	↑ testosterone possible	Adjust testosterone dose as needed based on clinical effects.
Immunosuppressants			
Cyclosporine, Sirolimus, Tacrolimus	ATV/c, ATV/r, DRV/c, DRV/r	↑ immunosuppressant expected	Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant and monitor for immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with a specialist as necessary.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Everolimus	DRV/c, DRV/r	↑ immunosuppressant expected	**Do not coadminister.**
	ATV/c, ATV/r	↑ immunosuppressant expected	Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant and monitor for immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with a specialist as necessary.
Lipid-Modifying			
Atorvastatin	ATV/r	↑ atorvastatin possible	Administer the lowest effective atorvastatin dose while monitoring for adverse events.
	ATV/c	Atorvastatin AUC ↑ 9.2-fold and C_{max} ↑ 18.9-fold	**Do not coadminister.**
	DRV/c	Atorvastatin AUC ↑ 3.9-fold and C_{max} ↑ 4.2-fold	Administer the lowest effective atorvastatin dose while monitoring for adverse events. Do not exceed 20 mg atorvastatin daily.
	DRV/r	DRV/r plus atorvastatin 10 mg similar to atorvastatin 40 mg administered alone	Administer the lowest effective atorvastatin dose while monitoring for adverse events. Do not exceed 20 mg atorvastatin daily.
Fluvastatin	ATV/c, DRV/c	↑ fluvastatin expected	Administer the lowest effective fluvastatin dose while monitoring for adverse events.
	ATV/r, DRV/r	↑ or ↓ fluvastatin possible	
Lomitapide	ATV/c, ATV/r, DRV/c, DRV/r	↑ lomitapide expected	**Contraindicated**
Lovastatin	ATV/c, ATV/r, DRV/c, DRV/r	Significant ↑ lovastatin expected	**Contraindicated**

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Pitavastatin	ATV/c, DRV/c	No data	No dose adjustment needed. Monitor for pitavastatin-related adverse events.
	ATV/r, DRV/r	**With ATV/r** • ↔ pitavastatin expected • ↔ ATV/r expected **With DRV/r** • ↓ pitavastatin AUC 26% • ↔ DRV/r	No dose adjustment needed
Pravastatin	ATV/c, ATV/r	No data	Administer the lowest effective pravastatin dose while monitoring for adverse events.
	DRV/c, DRV/r	**With DRV/r** • Pravastatin AUC ↑ 81% following single dose of pravastatin • Pravastatin AUC ↑ 23% at steady state	Administer the lowest effective pravastatin dose while monitoring for adverse events.
Rosuvastatin	ATV/r	Rosuvastatin AUC ↑ 3-fold and C_{max} ↑ 7-fold	Administer the lowest effective rosuvastatin dose while monitoring for adverse events. Do not exceed rosuvastatin 10 mg daily.
	ATV/c	Rosuvastatin AUC ↑ 3.4-fold and C_{max} ↑ 10.6-fold	
	DRV/c	Rosuvastatin AUC ↑ 1.9-fold and C_{max} ↑ 3.8-fold	Administer the lowest effective rosuvastatin dose while monitoring for adverse events. Do not exceed rosuvastatin 20 mg daily.
	DRV/r	Rosuvastatin AUC ↑ 48% and C_{max} ↑ 2.4-fold	Administer the lowest effective rosuvastatin dose while monitoring for adverse events.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Simvastatin	ATV/c, ATV/r, DRV/c, DRV/r	Significant ↑ simvastatin expected	**Contraindicated**
Narcotics and Treatment for Opioid Dependence			
Buprenorphine Sublingual, buccal, or implant	ATV/r	Buprenorphine AUC ↑ 66% Norbuprenorphine (active metabolite) AUC ↑ 105%	Monitor for sedation and other signs or symptoms of overmedication. Buprenorphine dose reduction may be necessary. It may be necessary to remove implant and treat with a formulation that permits dose adjustments.
	DRV/r	↔ buprenorphine Norbuprenorphine (active metabolite) AUC ↑ 46% and C_{min} ↑ 71%	No dose adjustment needed. Monitor for buprenorphine-related adverse events. When transferring buprenorphine from transmucosal delivery to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.
	ATV/c, DRV/c	↑ buprenorphine possible	Titrate buprenorphine dose using the lowest initial dose. Dose adjustment of buprenorphine may be needed. It may be necessary to remove implant and treat with a formulation that permits dose adjustments. Monitor for buprenorphine-related adverse events.
Fentanyl	ATV/c, ATV/r, DRV/c, DRV/r	↑ fentanyl possible	Monitor for fentanyl-related adverse events, including potentially fatal respiratory depression.
Lofexidine	ATV/c, ATV/r, DRV/c, DRV/r	↑ lofexidine possible	Monitor for lofexidine-related adverse events, including symptoms of orthostasis and bradycardia.
Methadone	ATV/c, DRV/c	No data	Titrate methadone dose using the lowest feasible initial dose. Dose adjustment of methadone may be needed. Monitor for methadone-related adverse events.
	ATV/r, DRV/r	ATV/r and DRV/r ↓ R-methadone[d] AUC 16% to 18%	Opioid withdrawal is unlikely but may occur. Monitor for opioid withdrawal and increase methadone dose as clinically indicated.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Oxycodone	ATV/c, ATV/r, DRV/c, DRV/r	↑ oxycodone expected	Monitor for opioid-related adverse events, including potentially fatal respiratory depression. Oxycodone dose reduction may be necessary.
Tramadol	ATV/c, ATV/r, DRV/c, DRV/r	↑ tramadol expected ↓ M1 (active metabolite) possible	Tramadol dose adjustments may be necessary. Monitor for clinical response and tramadol-related adverse events.
PDE5 Inhibitors			
Avanafil	ATV/c, ATV/r, DRV/c, DRV/r	RTV 600 mg twice daily (for 5 days) ↑ avanafil AUC 13-fold and ↑ C_{max} 2.4-fold	**Do not coadminister.**
Sildenafil	ATV/c, ATV/r, DRV/c, DRV/r	DRV/r plus sildenafil 25 mg similar to sildenafil 100 mg alone RTV 500 mg twice daily ↑ sildenafil AUC 1,000%	**For Treatment of Erectile Dysfunction** • Start with sildenafil 25 mg every 48 hours and monitor for sildenafil-related adverse events. **Contraindicated** for treatment of PAH.
Tadalafil	ATV/c, ATV/r, DRV/c, DRV/r	RTV 200 mg twice daily ↑ tadalafil AUC 124%	**For Treatment of Erectile Dysfunction** *As-Needed Use* • Start with tadalafil 5 mg and do not exceed a single dose of tadalafil 10 mg every 72 hours. Monitor for tadalafil-related adverse events. *Once-Daily Use* • Do not exceed tadalafil 2.5 mg once daily. Monitor for tadalafil-related adverse events. **For Treatment of PAH** *In Patients on a PI >7 Days* • Start with tadalafil 20 mg once daily and increase to tadalafil 40 mg once daily based on tolerability.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
			In Patients on Tadalafil Who Require a PI • Stop tadalafil ≥24 hours before PI initiation. Seven days after PI initiation, restart tadalafil at 20 mg once daily and increase to tadalafil 40 mg once daily based on tolerability. *In Patients Switching Between COBI and RTV* • Maintain tadalafil dose. **For Treatment of Benign Prostatic Hyperplasia** • Maximum recommended daily dose is tadalafil 2.5 mg per day. Monitor for tadalafil-related adverse events.
Vardenafil	ATV/c, ATV/r, DRV/c, DRV/r	RTV 600 mg twice daily ↑ vardenafil AUC 49-fold	Start with vardenafil 2.5 mg every 72 hours and monitor for vardenafil-related adverse events.
Sedative/Hypnotics			
Benzodiazepines			
Alprazolam, Clonazepam, Diazepam	ATV/c, ATV/r, DRV/c, DRV/r	↑ benzodiazepine possible RTV 200 mg twice daily (for 2 days) ↑ alprazolam half-life 222% and ↑ AUC 248%	Consider alternative benzodiazepines, such as lorazepam, oxazepam, or temazepam.
Lorazepam, Oxazepam, Temazepam	ATV/c, ATV/r, DRV/c, DRV/r	No data	These benzodiazepines are metabolized via non-CYP450 pathways and, therefore, have less interaction potential than other benzodiazepines.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Midazolam	ATV/c, ATV/r, DRV/c, DRV/r	↑ midazolam expected	Oral midazolam is **contraindicated** with PIs. Parenteral midazolam can be used with caution when given in a monitored situation with appropriate medical management available in case of respiratory sedation and/or prolonged sedation. Consider dose reduction, especially if more than a single dose of midazolam is administered.
Triazolam	ATV/c, ATV/r, DRV/c, DRV/r	↑ triazolam expected RTV 200 mg twice daily ↑ triazolam half-life 1,200% and ↑ AUC 2,000%	**Contraindicated**
Orexin Receptor Antagonist			
Daridorexant, Lemborexant, Suvorexant	ATV/c, ATV/r, DRV/c, DRV/r	↑ daridorexant, lemborexant, suvorexant expected	**Do not coadminister.**
Other Sedatives			
Eszopiclone	ATV/c, ATV/r, DRV/c, DRV/r	↑ eszopiclone expected	Start with lowest dose and increase to a maximum of 2 daily; monitor for eszopiclone-related adverse events.
Zolpidem	ATV/c, ATV/r, DRV/c, DRV/r	↑ zolpidem possible	Initiate zolpidem at a low dose and monitor for zolpidem-related adverse events. Dose reduction may be necessary.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Miscellaneous			
Calcifediol	ATV/c, ATV/r, DRV/c, DRV/r	↑ calcifediol possible	Dose adjustment of calcifediol may be required, and serum 25-hydroxyvitamin D, intact PTH, and serum calcium concentrations should be closely monitored.
Cisapride	ATV/c, ATV/r, DRV/c, DRV/r	↑ cisapride expected	**Contraindicated**
Colchicine	ATV/c, ATV/r, DRV/c, DRV/r	RTV 100 mg twice daily ↑ colchicine AUC 296% and C_{max} ↑ 184% Significant ↑ colchicine expected with all PIs, with or without COBI or RTV	**For Treatment of Gout Flares** • Administer a single dose of colchicine 0.6 mg, followed by colchicine 0.3 mg 1 hour later. Do not repeat dose for at least 3 days. **For Prophylaxis of Gout Flares** • If original dose was colchicine 0.6 mg twice daily, decrease to colchicine 0.3 mg once daily. If dose was 0.6 mg once daily, decrease to 0.3 mg every other day. **For Treatment of Familial Mediterranean Fever** • Do not exceed colchicine 0.6 mg once daily or colchicine 0.3 mg twice daily. **Contraindicated** in patients with hepatic (Child-Pugh Score A, B, or C) or renal impairment (CrCl <60 mL/min)
Dronabinol	ATV/c, ATV/r, DRV/c, DRV/r	↑ dronabinol possible	Monitor for dronabinol-related adverse events.
Eluxadoline	ATV/c, ATV/r, DRV/c, DRV/r	↑ eluxadoline expected	Administer eluxadoline at a dose of 75 mg twice daily and monitor for eluxadoline-related adverse events.
Finerenone	ATV/c, ATV/r, DRV/c, DRV/r	↑ finerenone expected	**Contraindicated**

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Flibanserin	ATV/c, ATV/r, DRV/c, DRV/r	↑ flibanserin expected	**Contraindicated**
Naloxegol	ATV/c, ATV/r, DRV/c, DRV/r	↑ naloxegol expected	**Contraindicated**
Praziquantel	ATV/c, ATV/r, DRV/c, DRV/r	↑ praziquantel possible	Consider alternative ARV. If coadministration is necessary, monitor for praziquantel-related adverse events.

[a] DHA is an active metabolite of artemether and artesunate.

[b] The following products contain no more than 30 mcg of ethinyl estradiol combined with norethindrone or norgestimate: Lo Minastrin Fe; Lo Loestrin Fe; Loestrin 1/20, 1.5/30; Loestrin Fe 1/20, 1.5/30; Loestrin 24 Fe; Minastrin 24 Fe; Ortho Tri-Cyclen Lo. Generic formulations also may be available.

[c] The following products contain at least 35 mcg of ethinyl estradiol combined with norethindrone or norgestimate: Brevicon; Femcon Fe; Modicon; Norinyl 1/35; Ortho-Cyclen; Ortho-Novum 1/35, 7/7/7; Ortho Tri-Cyclen; Ovcon 35; Tri-Norinyl. Generic formulations also may be available.

[d] R-methadone is the active form of methadone.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: 17-BMP = beclomethasone 17-monopropionate; ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; AST = aspartate aminotransferase; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; CCB = calcium channel blocker; CNS = central nervous system; COBI = cobicistat; CrCl = creatinine clearance; CMV = cytomegalovirus; CV = cardiovascular; CYP = cytochrome P; DHA = dihydroartemisinin; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DVT = deep vein thrombosis; ECG = electrocardiogram; eGFR = estimated glomerular filtration rate; EVG/c = elvitegravir/cobicistat; GI = gastrointestinal; H2RA = H2 receptor antagonist; HCV = hepatitis C virus; HRT = hormone replacement therapy; INR = international normalized ratio; LPV = lopinavir; LPV/r = lopinavir/ritonavir; MPA = medroxyprogesterone acetate; OATP = organic anion-transporting polypeptide; PAH = pulmonary arterial hypertension; PDE5 = phosphodiesterase type 5; PE = pulmonary embolism; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; PK = pharmacokinetic; PPI = proton pump inhibitor; PTH = parathyroid hormone; QTc = QT corrected for heart rate; RTV = ritonavir; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; TDF = tenofovir disoproxil fumarate; VPA = valproic acid

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Updated: September 12, 2024
Reviewed: September 12, 2024

This table provides information on the known or predicted interactions between non-nucleoside reverse transcriptase inhibitors (NNRTIs) and non-antiretroviral drugs. Cabotegravir (CAB) intramuscular (IM) plus rilpivirine (RPV) IM are co-packaged into a single product and are coadministered as a complete regimen; therefore, the dosing recommendations and clinical comments reflect the combination of CAB IM and RPV IM treatments. Drug interaction studies were not conducted with either CAB IM or RPV IM. Drug interaction studies with oral CAB and RPV were leveraged to make the dosing recommendations for CAB IM and RPV IM. For information regarding interactions between NNRTIs and other antiretroviral (ARV) drugs, including dosing recommendations, refer to Tables 24c, 24e, 24f, 25a, and 25b.

Recommendations for managing a particular drug interaction may differ, depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or if a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. When an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgment to select the most appropriate alternative medication.

Oral doses of RPV at 75 mg and 300 mg once daily (equivalent to 3 and 12 times the recommended dose) were associated with prolonged QTc (or QT corrected for heart rate) interval. Known and expected/theoretical pharmacokinetic interactions, resulting in increased RPV exposures, are included in this table due to the safety concern of QTc prolongation. There is limited information about the potential for pharmacodynamic interactions between RPV (in the absence of increased RPV exposures) and drugs that prolong the QTc interval; therefore, these are not included in this table.

Nevirapine (NVP) is no longer commonly used in clinical practice in the United States and is not included in this table. Please refer to the U.S. Food and Drug Administration product labels for information regarding drug interactions between NVP and concomitant medications. Information may also be found in archived versions of this guideline.

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Antacids	DOR, EFV	↔ NNRTI AUC	No dose adjustment needed
	ETR	↔ ETR expected	No dose adjustment needed
	RPV IM	↔ RPV expected	No dose adjustment needed
	RPV PO	↓ RPV expected when given simultaneously	Give antacids at least 2 hours before or at least 4 hours after RPV.
H2 Receptor Antagonists	DOR	↔ DOR expected	No dose adjustment needed
	EFV	↔ EFV AUC	No dose adjustment needed
	ETR	↔ ETR AUC	No dose adjustment needed
	RPV IM	↔ RPV expected	No dose adjustment needed

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	RPV PO	RPV AUC ↓ 76% when famotidine 40 mg is taken 2 hours prior	Give H2 receptor antagonists at least 12 hours before or at least 4 hours after RPV.
Proton Pump Inhibitors	DOR	↔ DOR AUC and C_{min}	No dose adjustment needed
	EFV	↔ EFV expected	
	ETR	**With Omeprazole 40 mg Daily** • ETR AUC ↑ 41%	
	RPV IM	↔ RPV expected	No dose adjustment needed
	RPV PO	**With Omeprazole 20 mg Daily** • RPV AUC ↓ 40% to 65% and C_{min} ↓ 33%	**Contraindicated**
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia			
Alfuzosin, Doxazosin, Silodosin, Terazosin	DOR, RPV IM, RPV PO	↔ alpha-adrenergic antagonists expected	No dose adjustment needed
	EFV, ETR	↓ alpha-adrenergic antagonists expected	Consider alternative ARV or alpha-antagonist therapy. If coadministration is necessary, monitor for therapeutic effectiveness of alpha antagonist.
Tamsulosin	DOR, RPV IM, RPV PO	↔ tamsulosin expected	No dose adjustment needed
	EFV, ETR	↓ tamsulosin expected	Monitor for therapeutic effectiveness of tamsulosin after 2–4 weeks. May need to increase dose to tamsulosin 0.8 mg once daily for patients who fail to respond to the 0.4-mg dose.
Antibacterials—Antimycobacterials			
Bedaquiline	DOR, RPV IM, RPV PO	↔ bedaquiline expected	No dose adjustment needed
	EFV, ETR	↓ bedaquiline possible	**Do not coadminister.**
Rifabutin	DOR	DOR AUC ↓ 50%	Increase DOR dose to 100 mg twice daily. No dose adjustment is needed for rifabutin.
	EFV	Rifabutin ↓ 38%	Increase rifabutin dose to 450–600 mg per day.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	ETR	↔ rifabutin and metabolite AUC ETR AUC ↓ 37%	**Do not coadminister** ETR plus PI/r with rifabutin. Use rifabutin 300 mg once daily if ETR is administered without PI/r.
	RPV IM	↓ RPV expected	**Contraindicated**
	RPV PO	**Rifabutin Plus RPV 50 mg PO Once Daily Compared to RPV 25 mg Once Daily Alone** • ↔ RPV AUC and C_{min}	Increase RPV dose to 50 mg PO once daily during coadministration. No dose adjustment for rifabutin is needed.
Rifampin	DOR	DOR AUC ↓ 88%	**Contraindicated.** After stopping rifampin, wait 4 weeks before initiating DOR**.**
	EFV	EFV AUC ↓ 26%	**Do not use** EFV 400 mg with rifampin. Maintain EFV dose at 600 mg once daily and monitor for virologic response.
	ETR	Significant ↓ ETR possible	**Do not coadminister.**
	RPV IM	↓ RPV possible	**Contraindicated**
	RPV PO	RPV AUC ↓ 80%	**Contraindicated**
Rifapentine	DOR	**Once-Weekly Rifapentine Plus Isoniazid and DOR 100 mg Twice Daily Compared to DOR 100 mg Twice Daily Alone** • DOR AUC ↓ 29%, C_{min} ↓ 31%	**Contraindicated.** After stopping rifapentine, wait 4 weeks before initiating DOR**.**
	EFV	**Daily Rifapentine (Max 600 mg) With EFV** • ↔ EFV **Weekly Rifapentine (Max 900 mg) With EFV** • ↔ EFV	No dose adjustment needed
	ETR	↓ ETR possible	**Do not coadminister.**
	RPV IM, RPV PO	↓ RPV possible	**Contraindicated**
Antibacterials—Macrolides			
Azithromycin	DOR, EFV, ETR, RPV IM, RPV PO	↔ azithromycin expected	No dose adjustment needed

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Clarithromycin	DOR	↔ clarithromycin expected ↑ DOR possible	Monitor for ARV tolerability if used in combination.
	EFV	Clarithromycin AUC ↓ 39%	Monitor for effectiveness, or consider alternative agent (e.g., azithromycin) for MAC prophylaxis and treatment.
	ETR	Clarithromycin AUC ↓ 39% ETR AUC ↑ 42%	Consider alternative macrolide (e.g., azithromycin) for MAC prophylaxis and treatment.
	RPV IM, RPV PO	↔ clarithromycin expected ↑ RPV possible	Consider alternative macrolide (e.g., azithromycin) for MAC prophylaxis and treatment. If coadministered, monitor for QTc prolongation.
Erythromycin	DOR	↑ DOR possible	Monitor for ARV tolerability if used in combination.
	EFV, ETR	↑ EFV and ETR possible ↓ erythromycin possible	Monitor for ARV tolerability and antibiotic efficacy if used in combination.
	RPV IM, RPV PO	↑ RPV possible	Consider alternative macrolide (e.g., azithromycin). If coadministered, monitor for QTc prolongation.
Anticoagulants			
Apixaban	DOR, RPV IM, RPV PO	↔ apixaban expected	No dose adjustment needed
	EFV, ETR	↓ apixaban possible	Consider alternative ARV or anticoagulant therapy.
Dabigatran, Edoxaban	DOR, EFV, ETR, RPV IM, RPV PO	↔ DOAC expected	No dose adjustment needed
Rivaroxaban	DOR, RPV IM, RPV PO	↔ rivaroxaban expected	No dose adjustment needed
	EFV, ETR	↓ rivaroxaban possible	Consider alternative ARV or anticoagulant therapy.
Warfarin	DOR, RPV IM, RPV PO	↔ warfarin expected	No dose adjustment needed
	EFV, ETR	↑ or ↓ warfarin possible	Monitor INR and adjust warfarin dose accordingly.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antidepressants, Anxiolytics, and Antipsychotics Also see the Sedative/Hypnotics section below.			
Antidepressants and Anxiolytics			
Bupropion	DOR, ETR, RPV IM, RPV PO	↔ bupropion expected	No dose adjustment needed
	EFV	Bupropion AUC ↓ 55%	Titrate bupropion dose based on clinical response.
Citalopram, Escitalopram	DOR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed
	EFV, ETR	↓ antidepressant possible	Titrate antidepressant dose based on clinical response.
Desvenlafaxine, Venlafaxine	DOR, EFV, ETR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed
Duloxetine	DOR, EFV, ETR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed
Fluoxetine, Fluvoxamine	DOR, EFV, ETR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed
Mirtazapine	DOR, RPV IM, RPV PO	↔ mirtazapine expected	No dose adjustment needed
	EFV, ETR	↓ mirtazapine possible	Monitor antidepressant effect. Titrate dose as necessary based on clinical response.
Nefazodone	DOR, RPV IM, RPV PO	↑ NNRTI possible	No dose adjustment needed
	EFV, ETR	↓ nefazodone expected ↑ NNRTI possible	Monitor antidepressant effect. Titrate dose as necessary based on clinical response.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Paroxetine	DOR, ETR, RPV IM, RPV PO	↔ paroxetine expected	No dose adjustment needed
	EFV	↔ EFV and paroxetine	No dose adjustment needed
Sertraline	DOR, RPV IM, RPV PO	↔ sertraline expected	No dose adjustment needed
	EFV	Sertraline AUC ↓ 39%	Monitor the antidepressant effect. Titrate dose as necessary based on clinical response.
	ETR	↓ sertraline possible	
Trazodone	DOR, RPV IM, RPV PO	↔ trazodone expected	No dose adjustment needed
	EFV, ETR	↓ trazodone possible	Monitor for therapeutic effectiveness of trazodone and titrate dose as necessary.
Tricyclic Antidepressants (e.g., amitriptyline, doxepin, nortriptyline)	DOR, EFV, ETR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed
Antipsychotics			
Aripiprazole	DOR, RPV IM, RPV PO	↔ aripiprazole expected	No dose adjustment needed
	EFV, ETR	↓ aripiprazole expected	Monitor for therapeutic effectiveness of antipsychotic. Consider doubling usual dose of aripiprazole over 1–2 weeks. Refer to aripiprazole prescribing information for dose recommendations.
Brexpiprazole	DOR, RPV IM, RPV PO	↔ brexpiprazole expected	No dose adjustment needed
	EFV, ETR	↓ brexpiprazole expected	Monitor for therapeutic effectiveness of antipsychotic. Consider doubling the usual dose of brexpiprazole and making further adjustments based on clinical response. Refer to brexpiprazole prescribing information.
Cariprazine	DOR, RPV IM, RPV PO	↔ cariprazine expected	No dose adjustment needed
	EFV, ETR	↓ cariprazine and ↑ or ↓ active metabolite possible	**Do not coadminister.**

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Iloperidone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Lumateperone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	**Do not coadminister.**
Lurasidone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Olanzapine, Olanzapine/ Samidorphan	DOR, ETR, RPV IM, RPV PO	↔ olanzapine expected	No dose adjustment needed
	EFV	↓ olanzapine possible	Monitor for therapeutic effectiveness of olanzapine.
Other Antipsychotics CYP3A4 Substrates (e.g., clozapine, haloperidol, perphenazine, risperidone, thioridazine)	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Pimavanserin	DOR, RPV IM, RPV PO	↔ pimavanserin expected	No dose adjustment needed
	EFV, ETR	↓ pimavanserin expected	**Do not coadminister.**
Pimozide	DOR, RPV IM, RPV PO	↔ pimozide expected	No dose adjustment needed
	EFV, ETR	↓ pimozide possible	Monitor for therapeutic effectiveness of pimozide.
Quetiapine	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Ziprasidone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Antifungals			
Fluconazole	DOR	↑ DOR possible	No dose adjustment needed
	EFV	↔ fluconazole expected ↔ EFV AUC	No dose adjustment needed
	ETR	ETR AUC ↑ 86%	No dose adjustment needed
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Ibrexafungerp	DOR, RPV PO	↑ NNRTI possible	No dose adjustment needed
	EFV, ETR	↓ ibrexafungerp expected ↑ NNRTI possible	**Do not coadminister.**
	RPV IM	↔ ibrexafungerp expected ↔ RPV IM expected	No dose adjustment needed
Isavuconazole	DOR	↑ DOR possible	No dose adjustment needed
	EFV, ETR	↓ isavuconazole possible	Monitor isavuconazole concentration and antifungal response. Dose adjustments for isavuconazole may be necessary.
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Itraconazole	DOR	↑ DOR possible	No dose adjustment needed
	EFV	**EFV With Itraconazole Solution** • Itraconazole and OH-itraconazole AUC, C_{max}, and C_{min} ↓ 37% to 44% **EFV With Itraconazole Capsules** • Itraconazole AUC ↓ 86% and OH-itraconazole AUC 84%	**Do not coadminister** unless potential benefits outweigh the risks. Failure to achieve therapeutic itraconazole concentrations has been reported. If coadministration is necessary, closely monitor itraconazole concentration and adjust dose accordingly.
	ETR	↓ itraconazole possible ↑ ETR possible	Dose adjustments for itraconazole may be necessary. Monitor itraconazole concentration and antifungal response.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Posaconazole	DOR, ETR	↑ NNRTI possible	No dose adjustment needed
	EFV	Posaconazole AUC ↓ 50% ↔ EFV AUC	**Do not coadminister** unless potential benefits outweigh the risks. If coadministration is necessary, monitor posaconazole concentration and adjust dose accordingly.
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Voriconazole	DOR	↑ DOR possible	No dose adjustment needed
	EFV	Voriconazole AUC ↓ 77% EFV AUC ↑ 44%	**Contraindicated at standard doses** Adjust dose to voriconazole 400 mg twice daily plus EFV 300 mg daily.
	ETR	↔ voriconazole AUC ETR AUC ↑ 36%	No dose adjustment needed
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Antimalarials			
Artemether/ Lumefantrine	DOR, RPV IM, RPV PO	↔ antimalarial expected	No dose adjustment needed
	EFV	Artemether AUC ↓ 79% DHA AUC ↓ 75% Lumefantrine AUC ↓ 30% to 56%	Consider alternative ARV or antimalarial drug. If used in combination, monitor closely for antimalarial efficacy.
	ETR	Artemether AUC ↓ 38% ↔ DHA AUC ↔ lumefantrine AUC ↔ ETR AUC	Clinical significance of the reduced antimalarial drug concentrations is unknown. If used in combination with ETR, monitor for antimalarial efficacy.
Atovaquone/Proguanil	DOR, ETR, RPV IM, RPV PO	No data	Monitor for antimalarial efficacy.
	EFV	Atovaquone AUC ↓ 75% Proguanil AUC ↓ 43%	No dose recommendation. Consider alternative drug for malaria prophylaxis, if possible.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antimigraine			
Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists			
Atogepant	DOR RPV IM, RPV PO	↔ atogepant expected	No dose adjustment needed
	EFV, ETR,	↓ atogepant possible	Episodic migraine: Increase atogepant dose to 30–60 mg once daily. Chronic migraine: **Do not coadminister.**
Rimegepant	DOR, RPV IM, RPV PO	↔ rimegepant expected	No dose adjustment needed
	EFV, ETR,	↓ rimegepant possible	Consider alternative ARV or migraine medication.
Ubrogepant	DOR, RPV IM, RPV PO	↔ ubrogepant expected	No dose adjustment needed
	EFV, ETR	↓ ubrogepant expected	Use initial dose of 100 mg, followed by second dose of 100 mg if needed.
Zavegepant	DOR, RPV IM, RPV PO	↔ zavegepant expected	No dose adjustment needed
	EFV, ETR,	↓ zavegepant possible	
Serotonin 5-HT1B, 1D Receptor Agonists			
Almotriptan, Eletriptan	DOR RPV IM, RPV PO	↔ almotriptan expected	No dose adjustment needed
	EFV, ETR,	↓ almotriptan possible	
Frovatriptan, Naratriptan, Rizatriptan, Sumatriptan, Zolmitriptan	DOR, EFV, ETR, RPV IM, RPV PO	↔ migraine medication expected	No dose adjustment needed
Antiplatelets			
Clopidogrel	DOR, RPV IM, RPV PO	↔ clopidogrel expected	No dose adjustment needed
	EFV, ETR	↓ activation of clopidogrel possible	Consider alternative ARV or antiplatelet. ETR may prevent metabolism of clopidogrel to its active metabolite.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Prasugrel	All NNRTIs	↔ prasugrel expected	No dose adjustment needed
Ticagrelor	DOR, RPV IM, RPV PO	↔ ticagrelor expected	No dose adjustment needed
	EFV, ETR	↓ ticagrelor expected	Consider alternative ARV or anticoagulant therapy.
Vorapaxar	DOR, RPV IM, RPV PO	↔ vorapaxar expected	No dose adjustment needed
	EFV, ETR	↓ vorapaxar expected	Insufficient data to make a dose recommendation.
Antipneumocystis and Antitoxoplasmosis			
Atovaquone (oral solution)	DOR, ETR, RPV IM, RPV PO	No data	Monitor for therapeutic effectiveness of atovaquone.
	EFV	Atovaquone AUC ↓ 44% to 47%	Consider alternative ARV or agent for PCP or toxoplasmosis treatment or prophylaxis. If coadministration is necessary, monitor for therapeutic effectiveness of atovaquone.
Antiseizure			
Carbamazepine, Phenobarbital, Phenytoin, Primidone	DOR	↓ DOR possible	**Contraindicated.** After stopping antiseizure medication, wait 4 weeks before initiating DOR.
	EFV	**Carbamazepine Plus EFV** • Carbamazepine AUC ↓ 27% • EFV AUC ↓ 36% **Phenytoin Plus EFV** • ↓ EFV • ↑ or ↓ phenytoin possible **Phenobarbital or Primidone Plus EFV** • ↓ EFV and antiseizure agent possible	Consider alternative ARV or antiseizure medication. If coadministration is necessary, monitor antiseizure drug and EFV concentrations.
	ETR	↓ antiseizure agent and ETR possible	**Do not coadminister.**
	RPV IM, RPV PO	↓ RPV possible	**Contraindicated**

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Eslicarbazepine	DOR, EFV, ETR, RPV IM, RPV PO	↓ NNRTI possible	Consider alternative ARV or antiseizure medication. If coadministration is necessary, monitor virologic response and consider monitoring plasma concentrations of ARVs.
Oxcarbazepine	DOR, RPV IM, RPV PO	↓ NNRTI possible	**Contraindicated**
	EFV, ETR	↓ NNRTI possible	Consider alternative ARV or antiseizure medication. If coadministration is necessary, monitor virologic response and consider monitoring plasma concentrations of ARVs.
Ethosuximide, Lacosamide, Tiagabine, Zonisamide	DOR, RPV IM, RPV PO	↔ antiseizure agent expected	No dose adjustment needed
	EFV, ETR	↓ antiseizure agent possible	Monitor seizure control. Consider anticonvulsant therapeutic drug monitoring.
Lamotrigine	DOR, ETR, RPV IM, RPV PO	↔ lamotrigine expected	No dose adjustment needed
	EFV	↓ lamotrigine possible	Monitor seizure control and plasma concentrations of lamotrigine.
Antivirals—Hepatitis C			
Elbasvir/Grazoprevir	DOR	↔ elbasvir and grazoprevir DOR AUC ↑ 56% and C_{min} ↑ 41%	No dose adjustment needed
	EFV	Elbasvir AUC ↓ 54% Grazoprevir AUC ↓ 83% ↔ EFV	**Contraindicated**
	ETR	↓ elbasvir and grazoprevir expected	**Do not coadminister.**
	RPV IM	↔ elbasvir and grazoprevir expected ↔ RPV expected	No dose adjustment needed
	RPV PO	↔ elbasvir and grazoprevir ↔ RPV AUC and C_{min}	No dose adjustment needed

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Glecaprevir/ Pibrentasvir	DOR	↑ DOR expected	No dose adjustment needed
	EFV	↓ glecaprevir and pibrentasvir expected	**Do not coadminister.**
	ETR	↓ glecaprevir and pibrentasvir possible	**Do not coadminister.**
	RPV IM	↔ glecaprevir and pibrentasvir expected ↑ RPV expected	No dose adjustment needed
	RPV PO	↔ glecaprevir and pibrentasvir RPV AUC ↑ 84%	No dose adjustment needed
Ledipasvir/Sofosbuvir	DOR	↔ ledipasvir and sofosbuvir ↔ DOR	No dose adjustment needed
	EFV	Ledipasvir AUC, C_{min}, and C_{max} ↓ 34% ↔ sofosbuvir	
	ETR	No significant effect expected	
	RPV IM	↔ ledipasvir, sofosbuvir, and RPV expected	
	RPV PO	↔ ledipasvir and sofosbuvir ↔ RPV	
Sofosbuvir/ Velpatasvir	DOR, RPV IM, RPV PO	No significant effect expected	No dose adjustment needed
	EFV	Velpatasvir AUC ↓ 43%, C_{max} ↓ 37%, and C_{min} ↓ 47%	**Do not coadminister.**
	ETR	↓ velpatasvir expected	**Do not coadminister.**
Sofosbuvir/ Velpatasvir/ Voxilaprevir	DOR, RPV IM, RPV PO	No significant effect expected	No dose adjustment needed.
	EFV	Velpatasvir AUC ↓ 43%, C_{max} ↓ 37%, and C_{min} ↓ 47% ↓ voxilaprevir expected	**Do not coadminister.**
	ETR	↓ voxilaprevir expected ↓ velpatasvir expected	**Do not coadminister.**

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antivirals—Miscellaneous (e.g., for CMV, Mpox)			
Brincidofovir	All NNRTIs	↔ brincidofovir expected	No dose adjustment needed
Cidofovir	All NNRTIs	↔ cidofovir expected	No dose adjustment needed
Maribavir	DOR, RPV IM, RPV PO	↔ maribavir expected	No dose adjustment needed
	EFV, ETR	↓ maribavir possible	
Tecovirimat	DOR, RPV PO	↓ DOR or RPV expected but not likely to be clinically relevant	No dose adjustment needed
	EFV, ETR	↔ EFV or ETR expected	No dose adjustment needed
	RPV IM	↓ RPV expected but not likely to be clinically relevant	No dose adjustment needed. If there is a concern for suboptimal RPV exposure, seek expert consultation. Do not initiate CAB/RPV IM during or within 2 weeks after tecovirimat treatment. (Refer to Table 24d for interaction with CAB.)
Antivirals—SARS-CoV-2			
Molnupiravir	All NNRTIs	↔ expected	No dose adjustment needed
Remdesivir	All NNRTIs	↔ expected	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	DOR	**With Ritonavir 100 mg Twice Daily** • DOR AUC ↑ 254%	No dose adjustment needed
	EFV, ETR, RPV PO, RPV IM	↔ expected	No dose adjustment needed
Cardiac Medications			
Beta-Blockers			
Atenolol, Metoprolol, Nebivolol	DOR, EFV, ETR, RPV IM, RPV PO	↔ beta-blocker expected	No dose adjustment needed

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Bisoprolol, Carvedilol	DOR, RPV IM, RPV PO	↔ beta-blocker expected	No dose adjustment needed
	EFV, ETR	↓ beta-blocker possible	No dose adjustment needed. Monitor blood pressure and heart rate and titrate to clinical effect.
Labetalol	DOR, RPV IM, RPV PO	↔ beta-blocker expected	No dose adjustment needed
	EFV, ETR	↑ beta-blocker possible	No dose adjustment needed. Monitor blood pressure and heart rate and adjust dose to achieve desired clinical effect.
Calcium Channel Blockers			
Dihydropyridine Calcium Channel Blockers (e.g., amlodipine, nifedipine)	DOR, RPV IM, RPV PO	↔ CCBs expected	No dose adjustment needed
	EFV, ETR	↓ CCBs possible	Titrate CCB dose based on clinical response.
Non-Dihydropyridine Calcium Channel Blockers (e.g., diltiazem, verapamil)	DOR, RPV IM, RPV PO	↔ CCBs expected ↑ NNRTI possible	No dose adjustment needed
	EFV	Diltiazem AUC ↓ 69% ↓ verapamil possible	Titrate diltiazem or verapamil dose based on clinical response.
	ETR	↓ diltiazem or verapamil possible	
Cardiac—Other			
Bosentan	DOR	↓ DOR possible	Consider alternative ARV or alternative to bosentan. If coadministration is necessary, monitor virologic response.
	EFV, ETR	↓ NNRTI possible ↓ bosentan possible	Consider alternative ARV or alternative to bosentan. If coadministration is necessary, monitor bosentan efficacy and virologic response.
	RPV IM, RPV PO	↓ RPV possible	Consider alternative ARV or alternative to bosentan. If coadministration is necessary, monitor virologic response.
Eplerenone	DOR, RPV IM, RPV PO	↔ eplerenone expected	No dose adjustment needed
	EFV, ETR	↓ eplerenone possible	Titrate eplerenone dose based on clinical response.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Ivabradine	DOR, RPV IM, RPV PO	↔ ivabradine expected	No dose adjustment needed
	EFV, ETR	↓ ivabradine expected	**Contraindicated**
Mavacamten	DOR, RPV IM, RPV PO	↔ mavacamten expected ↓ NNRTI possible	Consider alternative ARV or alternative to mavacamten. If coadministration is necessary, monitor virologic response.
	EFV, ETR	↓ mavacamten expected ↓ NNRTI possible	**Contraindicated**
Ranolazine	DOR, RPV IM, RPV PO	↔ ranolazine expected	No dose adjustment needed
	EFV, ETR	↓ ranolazine expected	**Contraindicated**
Corticosteroids			
Beclomethasone, Ciclesonide	DOR, EFV, ETR, RPV IM, RPV PO	↔ corticosteroid expected	No dose adjustment needed
Budesonide, Fluticasone, Mometasone	DOR, RPV IM, RPV PO	↔ corticosteroid expected	No dose adjustment needed
	EFV, ETR,	↓ corticosteroid possible	Monitor corticosteroid efficacy and titrate as needed. May consider alternative corticosteroid for long-term use.
Dexamethasone	DOR, EFV, ETR	↓ NNRTI possible	Consider alternative corticosteroid for long-term use. If dexamethasone is used with NNRTI, monitor virologic response.
	RPV IM, RPV PO	Significant ↓ RPV possible	**Contraindicated** with more than a single dose of dexamethasone.
Prednisone, Prednisolone	DOR, RPV IM, RPV PO	↔ corticosteroid expected	No dose adjustment needed
	EFV, ETR,	↓ corticosteroid possible	Monitor corticosteroid efficacy and titrate as needed. May consider alternative corticosteroid for long-term use.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Glucose-Lowering			
Linagliptin, Sitagliptin	DOR, RPV IM, RPV PO	↔ antihyperglycemic expected	No dose adjustment needed
	EFV, ETR	↓ antihyperglycemic possible	Monitor glycemic control.
Metformin	DOR	↔ metformin AUC DOR AUC ↓ 26% and C_{max} ↓ 24%	No dose adjustment needed
	EFV, ETR, RPV IM	↔ metformin expected	No dose adjustment needed
	RPV PO	↔ metformin AUC	No dose adjustment needed
Sodium-Glucose Cotransporter-2 Inhibitors (e.g., canagliflozin, dapagliflozin, empagliflozin)	DOR, EFV, ETR, RPV IM, RPV PO	↔ antihyperglycemic expected	No dose adjustment needed
Herbal Products			
St. John's Wort	DOR	↓ DOR expected	**Contraindicated.** After stopping St. John's Wort, wait 4 weeks before initiating DOR.
	EFV, ETR	↓ EFV or ETR expected	**Do not coadminister.**
	RPV IM, RPV PO	↓ RPV expected	**Contraindicated**
Hormonal Therapies—Contraceptives			
Injectable Contraceptives **Depot MPA**	DOR, ETR, RPV IM, RPV PO	↔ MPA expected	No dose adjustment needed
	EFV	↔ MPA	No dose adjustment needed. Refer to Women With HIV section for people on EFV and RIF.
Oral Contraceptives (e.g., desogestrel, drospirenone, ethinyl estradiol, levonorgestrel, norgestimate)	DOR	↔ ethinyl estradiol ↔ levonorgestrel ↔ drospirenone expected	No dose adjustment needed
	EFV	↔ ethinyl estradiol Etonogestrel (metabolite of oral desogestrel) C_{min} ↓ 61%	**When Used for Contraception** Use alternative ARV or contraceptive methods.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		Levonorgestrel (metabolite of oral norgestimate) AUC ↓ 83% Norelgestromin (metabolite of oral norgestimate) AUC ↓ 64% ↓ drospirenone possible	**When Used for Other Clinical Indications (e.g., Acne, Menstrual Cycle Regulation)** Monitor for clinical effectiveness of hormonal therapy.
	ETR	Ethinyl estradiol AUC ↑ 22% ↔ norethindrone ↓ drospirenone possible	No dose adjustment needed for regimens that do not contain drospirenone For drospirenone-containing regimens used for contraception, use alternative ARV or alternative contraceptive method. If using drospirenone for other clinical indications, monitor for clinical effectiveness of hormonal therapy.
	RPV IM	↔ ethinyl estradiol expected ↔ norethindrone expected ↔ drospirenone expected	No dose adjustment needed
	RPV PO	↔ ethinyl estradiol ↔ norethindrone ↔ drospirenone expected	No dose adjustment needed
Subdermal Implant Contraceptives (e.g., etonogestrel, levonorgestrel)	DOR, RPV IM, RPV PO	↔ etonogestrel expected ↔ levonorgestrel expected	No dose adjustment needed
	EFV	Etonogestrel AUC ↓ 63% to 82% Levonorgestrel AUC ↓ 42% to 47% **Levonorgestrel 300 mg Implant With 600 mg EFV Compared to Levonorgestrel 150 mg Implant** • Levonorgestrel AUC ↓ 34%	Use alternative ARV or contraceptive methods. Unintended pregnancies were observed in women who used EFV and levonorgestrel implant concomitantly.
	ETR	↓ etonogestrel possible ↓ levonorgestrel possible	Consider using alternative ARV or contraceptive methods.
Transdermal Contraceptives (e.g., ethinyl estradiol/ norelgestromin, ethinyl estradiol/levonorgestrel)	DOR, RPV IM, RPV PO	↔ ethinyl estradiol or norelgestromin expected	No dose adjustment needed
	EFV	↓ ethinyl estradiol or norelgestromin possible	Consider alternative ARV or contraceptive method.
	ETR	↓ ethinyl estradiol or norelgestromin possible	Consider alternative ARV or contraceptive method.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Vaginal Ring Contraceptives (e.g., etonogestrel/ethinyl estradiol, segesterone/ethinyl estradiol)	DOR, RPV IM, RPV PO	↔ etonogestrel and ethinyl estradiol expected ↔ segesterone and ethinyl estradiol expected	No dose adjustment needed
	EFV	Ethinyl estradiol (intravaginal ring) AUC ↓ 56% Etonogestrel (intravaginal ring) AUC ↓ 81%	Use alternative ARV or contraceptive method.
		↓ segesterone and ethinyl estradiol possible	Consider alternative ARV or contraceptive method.
	ETR	↓ etonogestrel and ethinyl estradiol possible ↓ segesterone and ethinyl estradiol possible	Consider alternative ARV or contraceptive method.
Emergency Contraceptives Levonorgestrel (oral)	DOR, RPV IM, RPV PO	↔ levonorgestrel expected	No dose adjustment needed.
	EFV	**Levonorgestrel 1.5 mg Plus 600 mg EFV** • Levonorgestrel AUC ↓ 58% **Levonorgestrel 3 mg Plus 600 mg EFV Compared to Levonorgestrel 1.5 mg Alone** • ↔ levonorgestrel AUC	Increase dose of levonorgestrel to 3 mg when used for emergency postcoital contraception.
	ETR	↓ levonorgestrel possible	Consider alternative ARV or contraceptive method.
Hormonal Therapies—Miscellaneous			
5-Alpha Reductase Inhibitors (e.g., dutasteride, finasteride)	DOR, RPV IM, RPV PO	↔ dutasteride and finasteride expected	No dose adjustment needed
	EFV, ETR	↓ dutasteride and finasteride possible	Monitor effects of testosterone. Titrate testosterone dose as necessary to achieve therapeutic goals.
Cyproterone, Goserelin Acetate, Leuprolide, Progestogens, Spironolactone	DOR, RPV IM, RPV PO	↔ hormonal concentrations expected	No dose adjustment needed
	EFV, ETR	↓ cyproterone and progestogens possible ↔ goserelin, leuprolide acetate, and spironolactone expected	Monitor effects of estrogen and antiandrogen therapy. Titrate dose as necessary to achieve therapeutic goals.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Estradiol	DOR, RPV IM, RPV PO	↔ estradiol expected	No dose adjustment needed
	EFV	Estradiol AUC ↓ 28% ↔ EFV AUC	Monitor effects of estrogen and therapy. Titrate dose as necessary to achieve therapeutic goals
	ETR	↓ estradiol possible	
Menopausal Hormone Replacement Therapy (e.g., conjugated estrogens, drospirenone, estradiol, medroxyprogesterone, progesterone)	DOR, RPV IM, RPV PO	↔ hormonal concentrations expected	No dose adjustment needed
	EFV, ETR	↓ estrogen possible with estradiol or conjugated estrogen (equine and synthetic) ↓ medroxyprogesterone possible ↓ micronized progesterone possible ↓ drospirenone possible See Contraceptives—Oral above for other progestin-NNRTI interactions	Monitor menopausal symptoms. Titrate to the dose of hormonal therapy that achieves menopausal symptom relief.
Testosterone	DOR, RPV IM, RPV PO	↔ testosterone expected	No dose adjustment needed
	EFV, ETR	↓ testosterone possible	Monitor effects of testosterone. Titrate testosterone dose as necessary to achieve therapeutic goals.
Immunosuppressants			
Cyclosporine	DOR, RPV IM, RPV PO	↔ cyclosporine expected ↑ NNRTI possible	No dose adjustment needed
	EFV, ETR	↓ cyclosporine possible	Increase in immunosuppressant dose may be necessary. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.
Everolimus, Sirolimus, Tacrolimus	DOR, RPV IM, RPV PO	↔ immunosuppressant expected	No dose adjustment needed
	EFV, ETR	↓ immunosuppressant possible	Increase in immunosuppressant dose may be necessary. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lipid-Modifying			
Atorvastatin	DOR	↔ atorvastatin AUC	No dose adjustment needed
	EFV, ETR	Atorvastatin AUC ↓ 32% to 43%	Adjust atorvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
	RPV IM	↔ atorvastatin expected	No dose adjustment needed
	RPV PO	↔ atorvastatin AUC	No dose adjustment needed
Fluvastatin	DOR, RPV IM, RPV PO	↔ fluvastatin expected	No dose adjustment needed
	EFV, ETR	↑ fluvastatin possible	Dose adjustments for fluvastatin may be necessary. Monitor for fluvastatin toxicity.
Lovastatin, Simvastatin	DOR, RPV IM, RPV PO	↔ lovastatin and simvastatin expected	No dose adjustment needed
	EFV	Simvastatin AUC ↓ 60% to 68% Simvastatin active metabolite AUC ↓ 60%	Adjust simvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
	ETR	↓ lovastatin possible ↓ simvastatin possible	Adjust lovastatin or simvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
Pitavastatin	DOR, ETR, RPV IM, RPV PO	↔ pitavastatin expected	No dose adjustment needed
	EFV	↔ pitavastatin AUC	No dose adjustment needed
Pravastatin	DOR, RPV IM, RPV PO	↔ pravastatin expected	No dose adjustment needed
	EFV	Pravastatin AUC ↓ 44%	Adjust statin dose according to lipid responses, but do not exceed the maximum recommended dose.
	ETR	↓ pravastatin possible	
Rosuvastatin	DOR, EFV, ETR, RPV IM, RPV PO	↔ rosuvastatin expected	No dose adjustment needed

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Narcotics and Treatment for Opioid Dependence			
Buprenorphine Sublingual or buccal	DOR, RPV IM, RPV PO	↔ buprenorphine expected	No dose adjustment needed
	EFV	Buprenorphine AUC ↓ 50% Norbuprenorphine (active metabolite) AUC ↓ 71%	No dose adjustment needed, monitor for withdrawal symptoms.
	ETR	Buprenorphine AUC ↓ 25%	No dose adjustment needed
Buprenorphine Implant	DOR, RPV IM, RPV PO	↔ buprenorphine expected	No dose adjustment needed
	EFV, ETR	No data	Clinical monitoring is recommended when NNRTI is initiated after insertion of buprenorphine implant.
Lofexidine	DOR, EFV, ETR, RPV IM, RPV PO	↔ lofexidine expected	No dose adjustment needed
Methadone	DOR	↔ methadone AUC DOR AUC ↓ 26%	No dose adjustment needed
	EFV	Methadone AUC ↓ 52%	Opioid withdrawal common; monitor and increase methadone dose as necessary.
	ETR	↔ methadone AUC	No dose adjustment needed
	RPV IM	↓ methadone AUC expected	No dose adjustment needed; monitor for withdrawal symptoms.
	RPV PO	↔ R-methadone[a] AUC	No dose adjustment needed; monitor for withdrawal symptoms.
PDE5 Inhibitors			
Avanafil, Tadalafil, Vardenafil	DOR, RPV IM, RPV PO	↔ PDE5 inhibitor expected	No dose adjustment needed
	EFV, ETR	↓ PDE5 inhibitor possible	May need to titrate dose based on clinical effect.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Sildenafil	DOR	↔ sildenafil expected	No dose adjustment needed
	EFV	↓ sildenafil possible	May need to titrate sildenafil dose based on clinical effect.
	ETR	Sildenafil AUC ↓ 57%	May need to titrate sildenafil dose based on clinical effect.
	RPV IM	↔ sildenafil expected	No dose adjustment needed
	RPV PO	↔ sildenafil AUC and C_{max}	No dose adjustment needed
Sedative/Hypnotics			
Benzodiazepines			
Alprazolam, Triazolam	DOR, RPV IM, RPV PO	↔ alprazolam or triazolam expected	No dose adjustment needed
	EFV, ETR	↓ alprazolam or triazolam possible	Monitor for therapeutic effectiveness of benzodiazepine.
Diazepam	DOR, RPV IM, RPV PO	↔ diazepam expected	No dose adjustment needed
	EFV	↓ diazepam possible	Monitor for therapeutic effectiveness of diazepam.
	ETR	↑ diazepam possible	Decreased dose of diazepam may be necessary. Monitor for diazepam toxicity.
Lorazepam	DOR, ETR, RPV IM, RPV PO	↔ lorazepam expected	No dose adjustment needed
	EFV	↔ lorazepam AUC	No dose adjustment needed
Midazolam	DOR	↔ midazolam AUC	No dose adjustment needed
	EFV	↑ or ↓ midazolam possible	Monitor for therapeutic effectiveness and toxicity of midazolam.
	ETR	Midazolam AUC ↓ 31% Midazolam active metabolite C_{max} ↑ 57%	Monitor for therapeutic effectiveness of midazolam.
	RPV IM, RPV PO	↔ midazolam expected	No dose adjustment needed
Orexin Receptor Antagonists			
Daridorexant	DOR, RPV IM, RPV PO	↔ daridorexant expected	No dose adjustment needed
	EFV	Daridorexant AUC ↓ 61%	**Do not coadminister.**
	ETR	↓ daridorexant possible	

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lemborexant, Suvorexant	DOR, RPV IM, RPV PO	↔ lemborexant expected	No dose adjustment needed
	EFV, ETR	↓ lemborexant possible	**Do not coadminister.**
Other Sedatives			
Eszopiclone, Zolpidem	DOR, RPV IM, RPV PO	↔ eszopiclone or zolpidem expected	No dose adjustment needed
	EFV, ETR	↓ eszopiclone or zolpidem possible	Monitor for therapeutic effectiveness of sedative and titrate to clinical effect.
Miscellaneous			
Finerenone	DOR, RPV IM, RPV PO	↔ finerenone expected	No dose adjustment needed
	EFV, ETR	↓ finerenone expected	Consider alternative ARV or alternative to finerenone. If coadministration is necessary, monitor finerenone efficacy.
Praziquantel	DOR, RPV IM, RPV PO	↔ praziquantel expected	No dose adjustment needed
	EFV	R-praziquantel and S-praziquantel AUC ↓ 74% to 75%	**Do not coadminister**. If coadministration is necessary, consider alternative ARVs.
	ETR	↓ praziquantel possible	**Do not coadminister.** If coadministration is necessary, consider alternative ARVs.

[a] R-methadone is the active form of methadone.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: ARV = antiretroviral; AUC = area under the curve; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; CAB = cabotegravir; CCB = calcium channel blocker; DAA = direct-acting antiviral; DHA = dihydroartemisinin; DOAC = direct oral anticoagulants; DOR = doravirine; EFV = efavirenz; ETR = etravirine; IM = intramuscular; INR = international normalized ratio; isoniazid = isonicotinic acid hydrazide; MAC = *Mycobacterium avium* complex; MPA = medroxyprogesterone acetate; CMV = cytomegalovirus; NNRTI = non-nucleoside reverse transcriptase inhibitor; OH-itraconazole = active metabolite of itraconazole; PCP = *Pneumocystis jirovecii* pneumonia; PDE5 = phosphodiesterase type 5; PI/r = protease inhibitor/ritonavir; PO = orally; QTc = QT corrected for heart rate; RPV = rilpivirine

Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Updated: September 12, 2024
Reviewed: September 12, 2024

This table provides information on the known or predicted interactions between nucleoside reverse transcriptase inhibitors (NRTIs) and non-antiretroviral drugs.

Recommendations for managing a particular drug interaction may differ depending on whether a new antiretroviral (ARV) drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgment to select the most appropriate alternative medication.

This table focuses on interactions with pharmacokinetic study data and interactions without study data but where there is a clinical recommendation. Interactions associated with zidovudine (ZDV) are **not** included in this table. Please refer to the U.S. Food and Drug Administration product labels for information regarding drug interactions between ZDV and other drugs.

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antibacterials—Antimycobacterials			
Rifabutin	3TC, ABC, FTC,	↔ expected	No dose adjustment needed
	TAF	↓ TAF possible	**Use with caution.** If coadministered, monitor virologic response.
	TDF	↔ AUC TFV	No dose adjustment needed
Rifampin	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	**TAF With Rifampin Compared With TDF Alone** • TFV-DP AUC ↑ 4.2-fold **TAF With Rifampin Compared With TAF Alone** • TAF AUC ↓ 55% • TFV-DP AUC ↓ 36% **TAF 25 mg Twice Daily With Rifampin Compared With TAF Once Daily Alone** • TAF AUC ↓ 14% • TFV-DP AUC ↓ 24%	**Use with caution.** If coadministered, monitor virologic response. Intracellular TFV-DP levels are higher when TAF is coadministered with rifampin than when TDF is administered alone, but clinical outcomes have not been studied.
	TDF	↔ AUC TFV	No dose adjustment needed

Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Rifapentine	3TC, ABC, FTC,	↔ expected	No dose adjustment needed
	TAF	↓ TAF possible	**Use with caution.** If coadministered, monitor virologic response.
	TDF	↔ AUC TFV	No dose adjustment needed
Antiretrovirals			
Capsid Inhibitor			
LEN (SQ and PO)	3TC, ABC, FTC	↔ 3TC, ABC, FTC, LEN expected	No dose adjustment needed
	TAF	TAF AUC ↑ 32% ↔ LEN	No dose adjustment needed
	TDF	TDF AUC ↑ 47% ↔ LEN	No dose adjustment needed
INSTIs			
DTG	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	↔ TAF AUC	No dose adjustment needed
	TDF	↔ TDF AUC ↔ DTG AUC	No dose adjustment needed
RAL	3TC, ABC, FTC, TAF	↔ expected	No dose adjustment needed
	TDF	RAL AUC ↑ 49%	No dose adjustment needed
PIs			
ATV/c, ATV/r	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	**TAF 10 mg With ATV/r** • TAF AUC ↑ 91% **TAF 10 mg With ATV/c** • TAF AUC ↑ 75%	No dose adjustment needed (use TAF 25 mg)
	TDF	**With ATV (Unboosted)** • ATV AUC ↓ 25% and C_{min} ↓ 23% to 40% (higher C_{min} with RTV than without RTV) • TFV AUC ↑ 24% to 37%	Use ATV 300 mg plus (RTV 100 mg or COBI 150 mg) daily when coadministering TDF 300 mg daily. If using TDF and an H2 receptor antagonist in an ART-experienced patient, use ATV 400 mg plus (RTV 100 mg or COBI 150 mg) daily. Monitor for TDF-associated toxicities.

Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
DRV/c	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	**TAF 25 mg With DRV/c** • ↔ TAF	No dose adjustment needed
	TDF	TFV ↑ possible	Monitor for TDF-associated toxicities.
DRV/r	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	**TAF 10 mg With DRV/r** • ↔ TAF AUC	No dose adjustment needed
	TDF	TFV AUC ↑ 22% and C_{min} ↑ 37%	Clinical significance is unknown. If coadministered, monitor for TDF-associated toxicities.
Antiseizure			
Carbamazepine, Oxcarbazepine, Phenobarbital, Phenytoin	ABC	↑ carbamazepine possible ↓ ABC possible with oxcarbazepine, phenobarbital, phenytoin	No dose adjustment needed
	3TC, FTC, TDF	↔ expected	No dose adjustment needed
	TAF	**With Carbamazepine** • TAF AUC ↓ 55% • ↓ TAF possible with other anticonvulsants	**Do not coadminister.**
Antivirals—Hepatitis C			
Glecaprevir/Pibrentasvir	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	↔ TFV AUC	No dose adjustment needed
	TDF	TFV AUC ↑ 29%	No dose adjustment needed
Ledipasvir/Sofosbuvir	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	TFV AUC ↑ 27%	No dose adjustment needed
	TDF	Ledipasvir ↑ TFV AUC 35% to 98% when TDF is given with various PIs and NNRTIs. Ledipasvir ↑ TFV C_{min} 55% to 80% when TDF is given with various PIs, NNRTIs, or INSTIs.	**Do not coadminister** with EVG/c, TDF, or FTC. If TDF is used, monitor for TDF toxicities. Consider using TAF in patients at risk of TDF-associated adverse events.

Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		Further ↑ TFV AUC and C_{max} possible when TDF, ledipasvir/sofosbuvir, and PIs are coadministered.	Consider using TAF or alternative HCV therapy in patients on TDF plus a PI/r or PI/c. The safety of increased TFV exposure with this combination has not been established.
Ribavirin	3TC	↔ 3TC AUC	No dose adjustment needed
	ABC, FTC, TAF	↔ expected	No dose adjustment needed
	TDF	**Ribavirin With Sofosbuvir 400 mg** • ↔ TFV AUC	No dose adjustment needed
Sofosbuvir/Velpatasvir	3TC, ABC, FTC, TAF	↔ expected	No dose adjustment needed
	TDF	TFV C_{max} ↑ 44% to 46% and AUC ↑ 40% when coadministered with various ARV combinations.	If TDF is used in these patients, monitor for TDF-related toxicities. Consider using TAF in patients at risk of TDF-related adverse events.
Sofosbuvir/Velpatasvir/ Voxilaprevir	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	TAF AUC ↑ 52% to 57%	No dose adjustment needed
	TDF	TFV C_{max} ↑ 48% and AUC ↑ 39% when coadministered with various ARV combinations.	Monitor for TDF-related toxicities. Consider using TAF in patients at risk of TDF-related adverse events.
Antivirals—Miscellaneous (e.g., for Herpesvirus, CMV, HBV, Mpox)			
Adefovir	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	↑ TFV possible	**Do not coadminister.** Serum concentrations of TDF and/or other renally eliminated drugs may increase.
	TDF	↔ TFV	**Do not coadminister.**
Brincidofovir	3TC, ABC, FTC, TAF, TDF	↔ brincidofovir expected	No dose adjustment needed
Cidofovir	3TC, ABC, FTC, TAF	↔ cidofovir expected	No dose adjustment needed
	TDF	↑ TDF and cidofovir possible	Potential for renal toxicity when TDF is given with a nephrotoxic agent, such as cidofovir. If concomitant use is necessary, closely monitor renal function.

Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Famciclovir	3TC, ABC, TAF, TDF	↔ expected	No dose adjustment needed
	FTC	↔ AUC FTC, famciclovir	No dose adjustment needed
Ganciclovir, Valganciclovir	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF, TDF	↑ ganciclovir or TFV possible	Monitor for dose-related toxicities.
Tecovirimat	3TC, ABC, FTC, TAF, TDF	↔ tecovirimat expected	No dose adjustment needed
Antivirals—SARS-CoV-2			
Molnupiravir	3TC, ABC, FTC, TAF, TDF	↔ expected	No dose adjustment needed
Remdesivir	3TC, ABC, FTC, TAF, TDF	↔ expected	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	3TC, ABC, FTC, TAF, TDF	↔ expected	No dose adjustment needed
Hormonal Therapies—Contraceptives			
Injectable Contraceptives Depot MPA	3TC, ABC, TAF	↔ expected	No dose adjustment needed
	FTC, TDF	↔ FTC AUC ↔ TFV AUC	No dose adjustment needed
Oral Contraceptives (e.g., desogestrel, drospirenone, ethinyl estradiol, levonorgestrel, norelgestromin, norgestimate, norgestrel)	3TC, ABC, FTC, TDF	↔ expected	No dose adjustment needed
	TAF	↔ ethinyl estradiol AUC ↔ norelgestromin AUC ↔ norgestrel AUC	No dose adjustment needed
Hormonal Therapies—Menopause			
17-β-estradiol	3TC, ABC, TAF	↔ expected	No dose adjustment needed
	FTC	FTC AUC ↓ 14% to 24%	
	TDF	TFV AUC ↓ 12% to 27%	

Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Estradiol Valerate	3TC, ABC, TAF	↔ expected	No dose adjustment needed
	FTC	↔ FTC AUC ↔ estradiol AUC	
	TDF	↔ TFV AUC ↔ estradiol	
Narcotics and Treatment for Opioid Dependence			
Buprenorphine	ABC, FTC	↔ expected	No dose adjustment needed
	3TC, TDF	↔ 3TC, TDF, and buprenorphine	No dose adjustment needed
	TAF	↔ TAF expected	No dose adjustment needed
Methadone	3TC, FTC, TAF, TDF	↔ expected	No dose adjustment needed
	ABC	Methadone clearance ↑ 22%	No dose adjustment needed
Miscellaneous			
Ethanol	ABC	ABC AUC ↑ 41%	No dose adjustment needed
Riociguat	3TC, FTC, TAF, TDF	↔ expected	No dose adjustment needed
	ABC	Riociguat AUC ↑ 200%	If coadministered, initiate riociguat at 0.5 mg three times daily and monitor for riociguat-related adverse effects (e.g., hypotension).
St. John's Wort	3TC, ABC, FTC, TDF	↔ expected	No dose adjustment needed
	TAF	↓ TAF possible	**Do not coadminister.**

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; COBI = cobicistat; CMV = cytomegalovirus; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; HBV = hepatitis B virus; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; MPA = medroxyprogesterone acetate; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; PO: oral; RAL = raltegravir; RTV = ritonavir; SQ = subcutaneous; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir; TFV-DP = tenofovir diphosphate

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Updated: September 12, 2024
Reviewed: September 12, 2024

This table provides information on the known or predicted interactions between integrase strand transfer inhibitors (INSTIs) (bictegravir [BIC], dolutegravir [DTG], elvitegravir [EVG], or raltegravir [RAL]) and non-antiretroviral drugs. EVG is always coadministered with cobicistat (COBI or c). Cabotegravir (CAB) intramuscular (IM) plus rilpivirine (RPV) IM are co-packaged into a single product and are coadministered as a complete regimen; therefore, the dosing recommendations and clinical comments reflect the combination of CAB IM and RPV IM treatments. Because drug interaction studies were not conducted with either IM CAB or RPV, dosing recommendations for the IM formulations are based on drug interaction studies using oral CAB and RPV. For information regarding interactions between INSTIs and other antiretroviral (ARV) drugs, including dosing recommendations, refer to Tables 24c, 24e, 24f, and 25b.

Recommendations for managing a particular drug interaction may differ, depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgment to select the most appropriate alternative medication.

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Al, Mg **+/–** **Ca-Containing Antacids** Please refer to the Miscellaneous Drugs section of this table for recommendations on use with other polyvalent cation products (e.g., Fe and Ca supplements, multivitamins).	BIC	**Al/Mg Hydroxide Antacid** • ↔ BIC AUC if antacid is administered 2 hours after BIC and under fasting conditions • BIC AUC ↓ 52% if antacid is administered 2 hours before BIC • BIC AUC ↓ 47% to 79% if administered simultaneously with antacid **$CaCO_3$ Antacid** • ↔ BIC AUC if administered with food • BIC AUC ↓ 33% if administered under fasting conditions	**With Antacids That Contain Al/Mg** • Administer antacids that contain Al/Mg at least 2 hours after or 6 hours before BIC. **With Antacids That Contain Ca** • Administer BIC and antacids that contain Ca together with food. • **Do not coadminister** BIC simultaneously with antacids that contain Ca on an empty stomach.
	CAB PO	CAB PO ↓ expected	**With Antacids That Contain Polyvalent Cations (Al, Mg, or Ca)** • Administer antacid products at least 2 hours before or 4 hours after taking CAB PO.
	CAB IM	↔ CAB IM expected	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	DTG	DTG AUC ↓ 74% if administered simultaneously with antacid DTG AUC ↓ 26% if administered 2 hours before antacid	Administer DTG at least 2 hours before or at least 6 hours after antacids that contain polyvalent cations.
	EVG/c	EVG AUC ↓ 40% to 50% if administered simultaneously with antacid EVG AUC ↓ 15% to 20% if administered 2 hours before or after antacid; ↔ with a 4-hour interval	Separate EVG/c and antacid administration by more than 2 hours.
	RAL	**Al/Mg Hydroxide Antacid** • RAL C_{min} ↓ 49% to 63% **$CaCO_3$ Antacid** • RAL 400 mg twice daily: C_{min} ↓ 32% • RAL 1,200 mg once daily: C_{min} ↓ 48% to 57%	**Do not coadminister** RAL and Al/Mg hydroxide antacids. Use alternative acid-reducing agent. **With $CaCO_3$ Antacids** • RAL 1,200 mg once daily: **Do not coadminister.** • RAL 400 mg twice daily: No dose adjustment or separation needed
H2-Receptor Antagonists	BIC, CAB (PO and IM), DTG, EVG/c	↔ INSTI	No dose adjustment needed
	RAL	RAL AUC ↑ 44% and C_{max} ↑ 60%	No dose adjustment needed
Proton Pump Inhibitors	BIC, CAB (PO and IM), DTG, EVG/c	↔ INSTI	No dose adjustment needed
	RAL	RAL AUC ↑ 37% and C_{min} ↑ 24%	No dose adjustment needed
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia			
Alfuzosin	BIC, CAB (PO and IM), DTG, RAL	↔ alfuzosin expected	No dose adjustment needed
	EVG/c	↑ alfuzosin expected	**Contraindicated**
Doxazosin	BIC, CAB (PO and IM), DTG, RAL	↔ doxazosin expected	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EVG/c	↑ doxazosin possible	Initiate doxazosin at lowest dose. Titrate based on doxazosin efficacy. Monitor blood pressure. Doxazosin dose reduction may be needed.
Tamsulosin	BIC, CAB (PO and IM), DTG, RAL	↔ tamsulosin expected	No dose adjustment needed
	EVG/c	↑ tamsulosin expected	**Do not coadminister** unless the benefits outweigh the risks. If coadministered, monitor blood pressure.
Terazosin	BIC, CAB (PO and IM), DTG, RAL	↔ terazosin expected	No dose adjustment needed
	EVG/c	↑ terazosin possible	Initiate terazosin at lowest dose. Titrate based on terazosin efficacy. Monitor blood pressure. Terazosin dose reduction may be necessary.
Silodosin	BIC, CAB (PO and IM), DTG, RAL	↔ silodosin expected	No dose adjustment needed
	EVG/c	↑ silodosin expected	**Contraindicated**
Antibacterials—Antimycobacterials			
Bedaquiline	BIC, CAB (PO and IM), DTG, RAL	↔ bedaquiline	No dosage adjustment needed
	EVG/c	↑ bedaquiline possible	**Do not coadminister** unless benefits outweigh risks. If coadministered, consider therapeutic drug monitoring and monitor for bedaquiline-related adverse effects, including hepatotoxicity and QTc prolongation.
Rifabutin	BIC	**Rifabutin 300 mg Once Daily** • BIC AUC ↓ 38% and C_{min} ↓ 56%	**Do not coadminister.**
	CAB PO	CAB PO AUC ↓ 23% and C_{min} ↓ 26% ↔ rifabutin	No dose adjustment needed
	CAB IM	↓ CAB IM and RPV expected ↔ rifabutin expected	**Contraindicated** due to ↓ RPV, which is co-packaged and coadministered with CAB IM.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	DTG	**Rifabutin 300 mg Once Daily** • ↔ DTG AUC and C_{min} ↓ 30%	No dose adjustment needed
	EVG/c	**Rifabutin 150 mg Every Other Day With EVG/c Once Daily Compared to Rifabutin 300 mg Once Daily Alone** • ↔ rifabutin AUC • 25-O-desacetyl-rifabutin AUC ↑ 625% • EVG AUC ↓ 21% and C_{min} ↓ 67%	**Do not coadminister.**
	RAL	↔ RAL AUC and C_{min} ↓ 20%	No dose adjustment needed
Rifampin	BIC	BIC AUC ↓ 75%	**Contraindicated**
	CAB PO	CAB PO AUC ↓ 59% and C_{min} ↓ 50%	**Contraindicated**
	CAB IM	CAB IM ↓ expected	**Contraindicated**
	DTG	**Rifampin With DTG 50 mg Twice Daily Compared to DTG 50 mg Twice Daily Alone** • DTG AUC ↓ 54% and C_{min} ↓ 72% **Rifampin With DTG 50 mg Twice Daily Compared to DTG 50 mg Once Daily Alone** • DTG AUC ↑ 33% and C_{min} ↑ 22%	Use DTG 50 mg twice daily (instead of DTG 50 mg once daily) in patients without suspected or documented INSTI-associated resistance mutations. Consider an alternative to rifampin, such as rifabutin, in patients with certain suspected or documented INSTI-associated resistance mutations.
	EVG/c	Significant ↓ EVG and COBI expected	**Contraindicated**
	RAL	**RAL 400 mg** • RAL AUC ↓ 40% and C_{min} ↓ 61% **Rifampin With RAL 800 mg Twice Daily Compared to RAL 400 mg Twice Daily Alone** • RAL AUC ↑ 27% and C_{min} ↓ 53%	Use RAL 800 mg twice daily instead of 400 mg twice daily. **Do not coadminister** RAL 1,200 mg once daily with rifampin. Monitor closely for virologic response or consider using rifabutin as an alternative rifamycin.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Rifapentine	BIC, EVG/c	Significant ↓ BIC, EVG, and COBI expected	**Do not coadminister.**
	CAB (PO and IM)	Significant ↓ CAB (PO and IM) expected	**Contraindicated**
	DTG	**Rifapentine 900 mg Once Weekly** • DTG AUC ↓ 26% and C_{min} ↓ 47% **Rifapentine 600 mg Once Daily With DTG 50 mg Twice Daily vs DTG 50 mg Once Daily Alone** • ↔ DTG AUC and C_{min}	With **once-weekly** rifapentine, DTG 50 mg daily may be used in patients with viral suppression on daily DTG. Monitor for virologic efficacy. **Do not coadminister** in patients who require twice-daily DTG. With **once-daily** rifapentine for 4 weeks (1HP), use DTG 50 mg twice daily. See Tuberculosis/HIV Coinfection for more on rifapentine and DTG use.
	RAL	**Rifapentine 900 mg Once Weekly** • RAL AUC ↑ 71% and C_{min} ↓ 12% **Rifapentine 600 mg Once Daily** • RAL C_{min} ↓ 41%	For once-weekly rifapentine and RAL 400 mg twice daily, no dose adjustment is needed. **Do not coadminister** with once-daily rifapentine.
Antibacterials—Macrolides			
Azithromycin	All INSTIs	↔ azithromycin expected	No dose adjustment needed
Clarithromycin	BIC	↑ BIC possible	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ clarithromycin expected	No dose adjustment needed
	EVG/c	↑ clarithromycin expected ↑ COBI possible	Reduce clarithromycin dose by 50% in patients with CrCl 50 to 60 mL/min. **Do not coadminister** in patients with CrCl <50 mL/min. Consider alternative ARV or use azithromycin.
Erythromycin	BIC	↑ BIC possible	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ erythromycin expected	No dose adjustment needed
	EVG/c	↑ erythromycin expected ↑ COBI possible	No data available for dose recommendation. Consider alternative ARV or use azithromycin.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anticoagulants			
Apixaban	BIC, CAB (PO and IM), DTG, RAL	↔ apixaban expected	No dose adjustment needed
	EVG/c	↑ apixaban expected	**Do not coadminister** in patients who require apixaban 2.5 mg twice daily. Reduce apixaban dose by 50% in patients who require apixaban 5 mg or 10 mg twice daily.
Dabigatran	BIC, CAB (PO and IM), DTG, RAL	↔ dabigatran expected	No dose adjustment needed
	EVG/c	↑ dabigatran expected **With COBI 150 mg Alone** • Dabigatran AUC ↑ 110% to 127%	**Reduction of Risk of Stroke and Systemic Embolism in Nonvalvular Atrial Fibrillation in Adult Patients** • CrCl >30 mL/min: no dose adjustment needed • CrCl ≤30 mL/min: **do not coadminister.** **Treatment and Reduction in the Risk of Recurrence of DVT and PE or Prophylaxis of DVT and PE Following Hip Replacement Surgery in Adult Patients** • CrCl ≥50 mL/min: no dose adjustment needed • CrCl <50 mL/min: **do not coadminister.**
Edoxaban	BIC, CAB (PO and IM), DTG, RAL	↔ edoxaban expected	No dose adjustment needed
	EVG/c	↑ edoxaban expected	**Stroke Prevention in Nonvalvular Atrial Fibrillation** • No dose adjustment needed **DVT and PE** • Administer edoxaban 30 mg once daily.
Rivaroxaban	BIC, CAB (PO and IM), DTG, RAL	↔ rivaroxaban expected	No dose adjustment needed
	EVG/c	↑ rivaroxaban expected	**Do not coadminister.**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Warfarin	BIC, CAB (PO and IM), DTG, RAL	↔ warfarin expected	No dose adjustment needed
	EVG/c	↑ or ↓ warfarin possible	Monitor INR and adjust warfarin dose accordingly.
Antidepressants, Anxiolytics, and Antipsychotics Also see the Sedative/Hypnotics section below			
Antidepressants, Anxiolytics			
Bupropion	BIC, CAB (PO and IM), DTG, RAL	↔ bupropion expected	No dose adjustment needed
	EVG/c	↑ bupropion possible	Titrate bupropion dose based on clinical response.
Buspirone	BIC, CAB (PO and IM), DTG, RAL	↔ buspirone expected	No dose adjustment needed
	EVG/c	↑ buspirone possible	Initiate buspirone at a low dose. Buspirone dose reduction may be needed.
Desvenlafaxine	All INSTIs	↔ desvenlafaxine expected	No dose adjustment needed
Duloxetine	BIC, CAB (PO and IM), DTG, RAL	↔ duloxetine expected	No dose adjustment needed
	EVG/c	↑ duloxetine possible	No dose adjustment needed
Mirtazapine	BIC, CAB (PO and IM), DTG, RAL	↔ mirtazapine expected	No dose adjustment needed
	EVG/c	↑ mirtazapine possible	Monitor for mirtazapine-related adverse events. Mirtazapine dose reduction may be necessary.
Nefazodone	BIC, CAB (PO and IM), DTG, RAL	↔ nefazodone expected	No dose adjustment needed
	EVG/c	↑ nefazodone expected	Consider alternative ARV or antidepressant.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Trazodone	BIC, CAB (PO and IM), DTG, RAL	↔ trazodone expected	No dose adjustment needed
	EVG/c	↑ trazodone possible	Titrate dose based on antidepressant response and monitor for trazodone-related adverse events.
Tricyclic Antidepressants (e.g., amitriptyline, desipramine, doxepin, imipramine, nortriptyline)	BIC, CAB (PO and IM), DTG, RAL	↔ TCA expected	No dose adjustment needed
	EVG/c	Desipramine AUC ↑ 65%	Initiate with lowest dose of TCA and titrate dose carefully.
		↑ TCA expected	Initiate with lowest dose of TCA. Titrate dose carefully based on antidepressant response and/or drug concentrations.
Selective Serotonin Reuptake Inhibitors (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, vortioxetine)	EVG/c	↔ sertraline	No dose adjustment needed
	EVG/c	↑ other SSRIs possible	Initiate with lowest dose of SSRI. Titrate dose carefully based on antidepressant response.
	BIC, CAB (PO and IM), DTG, RAL	↔ SSRI expected	No dose adjustment needed
Venlafaxine	BIC, CAB (PO and IM), DTG, RAL	↔ venlafaxine expected	No dose adjustment needed
	EVG/c	↑ venlafaxine possible	Monitor for venlafaxine-related adverse events.
Antipsychotics			
Aripiprazole	BIC, CAB (PO and IM), DTG, RAL	↔ aripiprazole expected	No dose adjustment needed
	EVG/c	↑ aripiprazole expected	Administer 25% of the usual aripiprazole dose. Titrate based on aripiprazole effectiveness and adverse events. Refer to aripiprazole label for dosing recommendations in patients who are known to be CYP2D6-poor metabolizers or who have major depressive disorder.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Brexpiprazole	BIC, CAB (PO and IM), DTG, RAL	↔ brexpiprazole expected	No dose adjustment needed
	EVG/c	↑ brexpiprazole expected	Administer 25% of the usual brexpiprazole dose. Titrate based on brexpiprazole effectiveness and adverse events. Refer to brexpiprazole label for dosing recommendations in patients who are known to be CYP2D6-poor metabolizers or who have major depressive disorder.
Cariprazine	BIC, CAB (PO and IM), DTG, RAL	↔ cariprazine expected	No dose adjustment needed
	EVG/c	↑ cariprazine expected	**Starting Cariprazine in a Patient Who Is Already Receiving EVG/c** • Administer cariprazine 1.5 mg on Day 1 and Day 3, with no dose given on Day 2. From Day 4 onward, administer cariprazine 1.5 mg daily. Dose can be increased to a maximum of cariprazine 3 mg daily. If EVG/c is withdrawn, cariprazine dose may need to be increased. **Starting EVG/c in a Patient Who Is Already Receiving Cariprazine** • For patients receiving cariprazine 3 mg or cariprazine 6 mg daily, reduce the dose by half. For patients receiving cariprazine 4.5 mg daily, reduce dose to cariprazine 1.5 mg or cariprazine 3 mg daily. For patients receiving cariprazine 1.5 mg daily, change to cariprazine 1.5 mg every other day. If EVG/c is withdrawn, cariprazine dose may need to be increased.
Iloperidone	BIC, CAB (PO and IM), DTG, RAL	↔ iloperidone expected	No dose adjustment needed
	EVG/c	↑ iloperidone expected	Decrease iloperidone dose by 50%.
Lumateperone	BIC, CAB (PO and IM), DTG, RAL	↔ lumateperone expected	No dose adjustment needed
	EVG/c	↑ lumateperone expected	**Do not coadminister.**
Lurasidone	BIC, CAB (PO and IM), DTG, RAL	↔ lurasidone expected	No dose adjustment needed
	EVG/c	↑ lurasidone expected	**Contraindicated**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Olanzapine, Olanzapine/ Samidorphan	All INSTIs	↔ olanzapine expected	No dose adjustment needed
	EVG/c	↔ olanzapine expected ↑ samidorphan possible	No dose adjustment needed
Other Antipsychotics CYP3A4 and/or CYP2D6 substrates (e.g., perphenazine, risperidone, thioridazine)	EVG/c	↑ antipsychotic possible	Initiate antipsychotic at a low dose. Antipsychotic dose reduction may be needed.
Pimavanserin	BIC, CAB (PO and IM), DTG, RAL	↔ pimavanserin expected	No dose adjustment needed
	EVG/c	↑ pimavanserin expected	Reduce pimavanserin dose to 10 mg.
Pimozide	BIC, CAB (PO and IM), DTG, RAL	↔ pimozide expected	No dose adjustment needed
	EVG/c	↑ pimozide expected	**Contraindicated**
Quetiapine	BIC, CAB (PO and IM), DTG, RAL	↔ quetiapine expected	No dose adjustment needed
	EVG/c	↑ quetiapine AUC expected	**Starting Quetiapine in a Patient Receiving EVG/c** • Start quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine efficacy and adverse events. **Starting EVG/c in a Patient Receiving a Stable Dose of Quetiapine** • Reduce quetiapine dose to 1/6 of the current dose. Closely monitor for quetiapine efficacy and adverse events.
Ziprasidone	BIC, CAB (PO and IM), DTG, RAL	↔ ziprasidone expected	No dose adjustment needed
	EVG/c	↑ ziprasidone possible	Monitor for ziprasidone-related adverse events.
Antifungals			
Ibrexafungerp	BIC, CAB (PO and IM), DTG, RAL	↔ ibrexafungerp expected	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EVG/c	↑ ibrexafungerp expected	Reduce ibrexafungerp dose to 150 mg twice daily.
Isavuconazole	BIC, CAB (PO and IM), DTG, RAL	↑ INSTI possible	No dose adjustment needed
	EVG/c	↑ isavuconazole expected ↑ or ↓ EVG and COBI possible	**Contraindicated**
Itraconazole	BIC	↑ BIC expected	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ itraconazole expected	No dose adjustment needed
	EVG/c	↑ itraconazole expected ↑ EVG and COBI possible	Consider monitoring itraconazole concentrations to guide dose adjustments. **Do not coadminister** with high itraconazole doses (>200 mg/day) unless guided by itraconazole concentrations.
Posaconazole	BIC	↑ BIC expected	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ posaconazole expected	No dose adjustment needed
	EVG/c	↑ EVG and COBI possible ↑ posaconazole possible	If coadministered, monitor posaconazole concentrations.
Voriconazole	BIC	↑ BIC possible	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ voriconazole expected	No dose adjustment needed
	EVG/c	↑ voriconazole expected ↑ EVG and COBI possible	**Do not coadminister** voriconazole and COBI, unless the benefit outweighs the risk. If coadministered, consider monitoring voriconazole concentrations and adjust dose accordingly.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antimalarials			
Artemether/ Lumefantrine	BIC	↔ antimalarial expected	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ antimalarial expected	No dose adjustment needed
	EVG/c	↑ artemether and lumefantrine possible	Monitor for artemether and lumefantrine-related adverse events, including QTc prolongation.
Artesunate	All INSTIs	↔ dihydroartemisinin expected	No dose adjustment needed
Atovaquone/ Proguanil	All INSTIs	↔ atovaquone/proguanil expected	No dose adjustment needed
Mefloquine	CAB (PO and IM), DTG, RAL	↔ mefloquine expected	No dose adjustment needed
	EVG/c	↑ mefloquine possible	Monitor for mefloquine-related adverse events, including psychiatric symptoms and QTc prolongation.
Antimigraine			
Ergot Derivatives	BIC, CAB (PO and IM), DTG, RAL	↔ dihydroergotamine, ergotamine, and methylergonovine expected	No dose adjustment needed
	EVG/c	↑ dihydroergotamine, ergotamine, and methylergonovine expected	**Contraindicated**
Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists			
Atogepant	BIC, CAB (PO and IM), DTG, RAL	↔ atogepant expected ↑ atogepant expected	No dose adjustment needed
	EVG/c	↑ atogepant expected	Chronic migraine: **Do not coadminister.** Episodic migraine: Administer atogepant at a dose of 10 mg once daily.
Rimegepant	BIC, CAB (PO and IM), DTG, RAL	↔ rimegepant expected	No dose adjustment needed
	EVG/c	↑ rimegepant expected	**Do not coadminister.**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Ubrogepant	BIC, CAB (PO and IM), DTG, RAL	↔ ubrogepant expected	No dose adjustment needed
	EVG/c	↑ ubrogepant expected	**Contraindicated**
Zavegepant	BIC, CAB (PO and IM), DTG, RAL	↔ zavegepant expected	No dose adjustment needed
	EVG/c	↑ zavegepant expected	**Do not coadminister.**
Serotonin 5-HT1B, 1D Receptor Agonist			
Almotriptan	BIC, CAB (PO and IM), DTG, RAL	↔ almotriptan expected	No dose adjustment needed
	EVG/c	↑ almotriptan expected	Administer single dose of almotriptan 6.25 mg. Maximum dose should not exceed 12.5 mg in a 24-hour period.
Eletriptan	BIC, CAB (PO and IM), DTG, RAL	↔ eletriptan expected	No dose adjustment needed
	EVG/c	↑ eletriptan expected	**Contraindicated**
Frovatriptan, Naratriptan, Rizatriptan, Sumatriptan Zolmitriptan	All INSTIs	↔ triptan expected	No dose adjustment needed
Antiplatelets			
Clopidogrel	BIC, CAB (PO and IM), DTG, RAL	↔ clopidogrel expected	No dose adjustment needed
	EVG/c	↓ clopidogrel active metabolite, with impaired platelet inhibition expected	**Do not coadminister.**
Prasugrel	BIC, CAB (PO and IM), DTG, RAL	↔ prasugrel expected	No dose adjustment needed
	EVG/c	↓ prasugrel active metabolite, with no impairment of platelet inhibition expected	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Ticagrelor	BIC, CAB (PO and IM), DTG, RAL	↔ ticagrelor expected	No dose adjustment needed
	EVG/c	↑ ticagrelor expected	**Do not coadminister.**
Vorapaxar	BIC, CAB (PO and IM) DTG, RAL	↔ vorapaxar expected	No dose adjustment needed
	EVG/c	↑ vorapaxar expected	**Do not coadminister.**
Antipneumocystis and Antitoxoplasmosis			
Atovaquone	All INSTIs	↔ atovaquone expected	No dose adjustment needed
Antiseizure			
Carbamazepine	BIC	↓ BIC possible	**Do not coadminister.**
	CAB (PO and IM)	↓ CAB expected	**Contraindicated**
	DTG	DTG AUC ↓ 49%	Increase DTG dose to 50 mg twice daily in ART-naive or ART-experienced (but INSTI-naive) patients. **Do not coadminister** in INSTI-experienced patients with known or suspected INSTI resistance.
	EVG/c	Carbamazepine AUC ↑ 43% EVG AUC ↓ 69% and C_{min} ↓ >99% ↓ COBI expected	**Contraindicated**
	RAL	↓ or ↔ RAL possible	**Do not coadminister.**
Eslicarbazepine	All INSTIs	↓ INSTI possible ↓ COBI possible	Consider alternative ARV or anticonvulsant.
Ethosuximide	BIC, CAB (PO and IM), DTG, RAL	↔ ethosuximide expected	No dose adjustment needed
	EVG/c	↑ ethosuximide possible	Monitor for ethosuximide-related adverse events.
Lamotrigine	BIC, CAB (PO and IM), DTG, RAL	↔ lamotrigine expected	No dose adjustment needed
	EVG/c	No data	Monitor anticonvulsant concentrations and adjust dose accordingly.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Oxcarbazepine	BIC, DTG	↓ BIC and DTG possible	**Do not coadminister.**
	CAB (PO and IM)	↓ CAB expected	**Contraindicated**
	EVG/c, RAL	↓ EVG/c and RAL possible	Consider alternative ARV or anticonvulsant.
Phenobarbital, Phenytoin, Primidone	BIC, DTG, RAL	↓ BIC and DTG possible ↓ or ↔ RAL possible	**Do not coadminister.**
	CAB (PO and IM), EVG/c	↓ CAB and EVG/c expected	**Contraindicated**
Valproic Acid	DTG	DTG ↓ possible	No dose adjustment needed. Take with food and monitor virologic response.
	BIC, CAB (PO and IM), RAL	No data	No dose adjustment needed. Monitor virologic response.
Antivirals—Hepatitis C			
Elbasvir/ Grazoprevir	BIC	↔ BIC expected	No dose adjustment needed
	CAB (PO and IM)	↔ CAB, elbasvir, and grazoprevir expected	No dose adjustment needed
	DTG	↔ DTG ↔ elbasvir ↔ grazoprevir	No dose adjustment needed
	EVG/c	↑ elbasvir expected ↑ grazoprevir expected	**Do not coadminister.**
	RAL	↔ RAL with elbasvir RAL AUC ↑ 43% with grazoprevir ↔ elbasvir ↔ grazoprevir	No dose adjustment needed
Glecaprevir/ Pibrentasvir	BIC, CAB (PO and IM)	↔ BIC or CAB expected	No dose adjustment needed
	DTG	↔ DTG and glecaprevir/ pibrentasvir	No dose adjustment needed
	RAL	No significant effect RAL AUC ↑ 47%	

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EVG/c	Glecaprevir AUC ↑ 3-fold Pibrentasvir AUC ↑ 57% EVG AUC ↑ 47%	No dose adjustment needed If coadministered with TDF, monitor for TDF-related adverse events. Consider monitoring for hepatotoxicity if coadministered with TDF or TAF.
Ledipasvir/ Sofosbuvir	BIC, DTG, RAL	↔ BIC, DTG, and RAL	No dose adjustment needed
	CAB (PO and IM)	↔ CAB expected	No dose adjustment needed
	EVG/c/ TDF/FTC	↑ TDF expected ↑ ledipasvir expected	**Do not coadminister.**
	EVG/c/ TAF/FTC	↔ EVG/c/TAF/FTC expected	No dose adjustment needed
Sofosbuvir	BIC, CAB (PO and IM), DTG, EVG/C	↔ INSTI expected ↔ sofosbuvir expected	No dose adjustment needed
	RAL	↔ RAL and sofosbuvir	No dose adjustment needed
Sofosbuvir/ Velpatasvir	BIC, DTG, RAL	↔ sofosbuvir and velpatasvir	No dose adjustment needed. If coadministered with TDF, monitor for TDF-related adverse events.
	CAB (PO and IM)	↔ CAB expected ↔ sofosbuvir and velpatasvir expected	
	EVG/c	↔ EVG/c/TAF/FTC Velpatasvir AUC ↑ 50%	
Sofosbuvir/ Velpatasvir/ Voxilaprevir	BIC	**When Administered With Sofosbuvir/Velpatasvir/ Voxilaprevir (400 mg/ 100 mg/100 mg) Plus Voxilaprevir 100 mg** • ↔ BIC, sofosbuvir, velpatasvir, voxilaprevir	No dose adjustment needed
	EVG/c	**When Administered With Sofosbuvir/Velpatasvir/ Voxilaprevir (400 mg/ 100 mg/100 mg) Plus Voxilaprevir 100 mg** • Sofosbuvir AUC ↑ 22% • ↔ velpatasvir • Voxilaprevir AUC ↑ 2-fold	No dose adjustment needed. If coadministered with TDF, monitor for TDF-related adverse events. Consider monitoring for hepatotoxicity if coadministered with TDF or TAF.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ sofosbuvir, velpatasvir, and voxilaprevir expected	No dose adjustment needed
Antivirals—Miscellaneous (e.g., for CMV, Mpox)			
Brincidofovir	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI expected	No dose adjustment needed
	EVG/c	↑ brincidofovir possible ↑ EVG possible	Administer EVG/c dose at least 3 hours after administering brincidofovir and monitor for brincidofovir-related adverse events, including elevations in ALT/AST and bilirubin and GI adverse events.
Cidofovir	BIC, CAB (PO and IM), DTG, EVG/c, RAL	↔ INSTI expected ↔ cidofovir expected	No dose adjustment needed
Tecovirimat	CAB (IM)	↔ CAB expected	No dose adjustment needed Do not initiate CAB/RPV IM during or within 2 weeks after tecovirimat treatment. (Refer to Table 24b for interaction with RPV.)
	BIC, CAB (PO), DTG, EVG/c, RAL	↔ INSTI expected	No dose adjustment needed
Antivirals—SARS-CoV-2			
Molnupiravir	BIC, CAB (PO and IM), DTG, EVG/c, RAL	↔ INSTI and molnupiravir expected	No dose adjustment needed
Ritonavir-boosted Nirmatrelvir	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI and ritonavir-boosted nirmatrelvir expected	No dose adjustment needed.
	EVG/c/ FTC/TAF	↑ TAF possible ↔ ritonavir-boosted nirmatrelvir expected	No dose adjustment needed
Remdesivir	BIC, CAB (PO and IM), DTG, EVG/c, RAL	↔ INSTI and remdesivir expected	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Beta-Agonists, Long-Acting Inhaled			
Arformoterol, Formoterol	All INSTIs	↔ arformoterol or formoterol expected	No dose adjustment needed
Indacaterol	BIC, CAB (PO and IM), DTG, RAL	↔ indacaterol expected	No dose adjustment needed
	EVG/c	↑ indacaterol expected	
Olodaterol	BIC, CAB (PO and IM), DTG, RAL	↔ olodaterol expected	No dose adjustment needed
	EVG/c	↑ olodaterol expected	
Salmeterol	BIC, CAB (PO and IM), DTG, RAL	↔ salmeterol expected	No dose adjustment needed
	EVG/c	↑ salmeterol possible	**Do not coadminister** due to the potential for increased risk of salmeterol-associated cardiovascular events.
Cardiac Medications			
Antiarrhythmics			
Amiodarone	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ amiodarone expected	No dose adjustment needed
	EVG/c	↑ amiodarone expected	**Do not coadminister** unless the benefits outweigh the risks. If coadministration is necessary, monitor for amiodarone-related adverse events and consider monitoring ECG and amiodarone concentrations.
Digoxin	BIC, CAB (PO and IM), RAL	↔ digoxin expected	No dose adjustment needed
	EVG/c	Digoxin C_{max} ↑ 41% and ↔ AUC	Therapeutic drug monitoring for digoxin is recommended if available.
Dofetilide	CAB (PO and IM)	↔ dofetilide expected	No dose adjustment needed
	BIC, DTG	↑ dofetilide expected	**Contraindicated**
	EVG/c	↑ dofetilide possible	**Do not coadminister.**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Disopyramide	BIC, CAB (PO and IM), RAL	↔ disopyramide expected	No dose adjustment needed
	DTG	↑ disopyramide possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor disopyramide concentrations and for antiarrhythmic-related adverse events.
	EVG/c	↑ disopyramide expected	**Do not coadminister.**
Dronedarone	BIC, CAB (PO and IM), DTG, RAL	↔ dronedarone expected	No dose adjustment needed
	EVG/c	↑ dronedarone expected	**Contraindicated**
Flecainide	BIC, CAB (PO and IM), DTG, RAL	↔ flecainide expected	No dose adjustment needed
	EVG/c	↑ flecainide possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor flecainide concentrations and for antiarrhythmic-related adverse events.
Propafenone	BIC, CAB (PO and IM), DTG, RAL	↔ propafenone expected	No dose adjustment needed
	EVG/c	↑ propafenone possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor propafenone concentrations and for antiarrhythmic-related adverse events.
Mexiletine	BIC, CAB (PO and IM), DTG, RAL	↔ mexiletine expected	No dose adjustment needed
	EVG/c	↑ mexiletine possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor mexiletine concentrations and for antiarrhythmic-related adverse events.
Systemic Lidocaine	BIC, CAB (PO and IM), DTG, RAL	↔ lidocaine expected	No dose adjustment needed
	EVG/c	↑ lidocaine possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor lidocaine concentrations and for antiarrhythmic-related adverse events.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Quinidine	BIC, CAB (PO and IM), DTG, RAL	↔ quinidine expected	No dose adjustment needed
	EVG/c	↑ quinidine possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor quinidine concentrations and for antiarrhythmic-related adverse events.
Beta-Blockers			
Atenolol, Bisoprolol, Carvedilol, Metoprolol, Nadolol, Nebivolol, Sotalol	CAB (PO and IM), RAL	↔ beta-blocker expected	No dose adjustment needed
	BIC, DTG, EVG/c	↑ beta-blocker possible	Beta-blocker dose may need to be decreased; adjust dose based on clinical response.
Calcium Channel Blockers			
Calcium Channel Blockers	BIC	↑ BIC possible with diltiazem ↔ expected for all other CCBs	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ CCB expected	No dose adjustment needed
	EVG/c	↑ CCB possible	Titrate CCB dose and monitor for CCB efficacy and adverse events.
Cardiac—Other			
Bosentan	BIC, DTG	↓ BIC and DTG possible	No dose adjustment needed
	CAB (PO and IM)	↔ bosentan expected	Consider using alternative ARV or an alternative to bosentan because bosentan may ↓ RPV, which is co-packaged and coadministered with CAB IM. If bosentan is used with RPV, monitor virologic response to ART.
	RAL	↔ bosentan expected	No dose adjustment needed
	EVG/c	↑ bosentan possible	**In Patients on EVG/c ≥10 Days** • Start bosentan at 62.5 mg once daily or every other day based on individual tolerability. **In Patients on Bosentan Who Require EVG/c** • Stop bosentan ≥36 hours before EVG/c initiation. At least 10 days after initiation of EVG/c, resume bosentan at 62.5 mg once daily or every other day based on individual tolerability.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Eplerenone	BIC, CAB (PO and IM), DTG, RAL	↔ eplerenone expected	No dose adjustment needed
	EVG/c	↑ eplerenone expected	**Contraindicated**
Ivabradine	BIC, CAB (PO and IM), DTG, RAL	↔ ivabradine expected	No dose adjustment needed
	EVG/c	↑ ivabradine expected	**Contraindicated**
Mavacamten	BIC, CAB (PO and IM), DTG, RAL	↔ mavacamten expected	No dose adjustment needed
	EVG/c	↑ mavacamten expected	**Contraindicated**
Ranolazine	BIC, CAB (PO and IM), DTG, RAL	↔ ranolazine expected	No dose adjustment needed
	EVG/c	↑ ranolazine expected	**Contraindicated**
Corticosteroids			
Beclomethasone Inhaled or intranasal	BIC, CAB (PO and IM), DTG, EVG/c, RAL	↔ glucocorticoid expected	No dose adjustment needed
Budesonide, Ciclesonide, Fluticasone, Mometasone Inhaled or intranasal	BIC, CAB (PO and IM), DTG, RAL	↔ glucocorticoid expected	No dose adjustment needed
	EVG/c	↑ glucocorticoid possible	**Do not coadminister** unless the potential benefits of inhaled or intranasal corticosteroid outweigh the risks of systemic corticosteroid adverse effects. Coadministration can result in adrenal insufficiency and Cushing's syndrome. Consider using an alternative corticosteroid (e.g., beclomethasone).
Betamethasone, Budesonide Systemic	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ glucocorticoid expected	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EVG/c	↑ glucocorticoid possible ↓ EVG possible	**Do not coadminister** unless the potential benefits of systemic budesonide outweigh the risks of systemic corticosteroid adverse effects. Coadministration can result in adrenal insufficiency and Cushing's syndrome.
Dexamethasone Systemic	BIC	↓ BIC possible	Consider alternative corticosteroid for long-term use or alternative ARV. If coadministration is necessary, monitor virologic response to ART.
	CAB (PO and IM), DTG, RAL	↔ INSTI expected	No dose adjustment needed
	EVG/c	↓ EVG and COBI possible	Consider alternative corticosteroid for long-term use or alternative ARV. If coadministration is necessary, monitor virologic response to ART.
Prednisone, Prednisolone Systemic	BIC, CAB (PO and IM), DTG, RAL	↔ glucocorticoid expected	No dose adjustment needed
	EVG/c	↑ prednisolone possible	Coadministration may be considered if the potential benefits outweigh the risks of systemic corticosteroid adverse effects. If coadministration is necessary, monitor for adrenal insufficiency and Cushing's syndrome.
Betamethasone, Methylprednisolone, Prednisolone, Triamcinolone Local injections, including intra-articular, epidural, or intra-orbital	BIC, CAB (PO and IM), DTG, RAL	↔ glucocorticoid expected	No dose adjustment needed
	EVG/c	↑ glucocorticoid expected	**Do not coadminister.** Coadministration may result in adrenal insufficiency and Cushing's syndrome.
Glucose-Lowering			
Metformin	BIC	Metformin AUC ↑ 39%	Monitor for adverse events of metformin.
	CAB (PO and IM), RAL	↔ metformin expected	No dose adjustment needed
	DTG	**DTG 50 mg Once Daily Plus Metformin 500 mg Twice Daily** • Metformin AUC ↑ 79% and C_{max} ↑ 66%	Start metformin at the lowest dose and titrate based on glycemic control. Monitor for adverse events of metformin. When starting/stopping DTG in patients on metformin, dose adjustment of metformin may be necessary to maintain optimal glycemic control and/or minimize adverse events of metformin.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		DTG 50 mg Twice Daily Plus Metformin 500 mg Twice Daily • Metformin AUC ↑ 2.4-fold and C_{max} ↑ 2-fold	
	EVG/c	↑ metformin possible	No dose adjustment needed
Saxagliptin	BIC, CAB (PO and IM), DTG, RAL	↔ saxagliptin expected	No dose adjustment needed
	EVG/c	↑ saxagliptin expected	Limit saxagliptin dose to 2.5 mg once daily.
Dapagliflozin/ Saxagliptin	BIC, CAB (PO and IM), DTG, RAL	↔ dapagliflozin or saxagliptin expected	No dose adjustment needed
	EVG/c	↑ saxagliptin expected	**Do not coadminister.** Dapagliflozin is available only as a coformulated drug that contains 5 mg of saxagliptin. When coadministered with EVG/c, the dose of saxagliptin should not exceed 2.5 mg once daily; thus, this combination **is not recommended.**
Herbal Products			
St. John's Wort	BIC, CAB (PO and IM), DTG	↓ BIC and DTG possible	**Do not coadminister.**
	EVG/c	↓ EVG and COBI expected	**Contraindicated**
Hormonal Therapies			
Injectable Contraceptives **Depot MPA**	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI and injectable contraceptive expected	No dose adjustment needed
	EVG/c	↑ MPA possible	No dose adjustment needed
Oral Contraceptives (e.g., desogestrel, drospirenone, ethinyl estradiol, levonorgestrel, norethindrone, norgestimate)	BIC, CAB (PO, IM), DTG, RAL	↔ ethinyl estradiol and norgestimate with DTG ↔ ethinyl estradiol and levonorgestrel with CAB PO ↔ ethinyl estradiol and norgestimate expected with BIC, RAL ↔ norgestimate expected with CAB PO and IM	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		↔ levonorgestrel expected ↔ drospirenone expected ↔ norethindrone expected	
	EVG/c	Norgestimate AUC, C_{max}, and C_{min} ↑ > 2-fold Ethinyl estradiol AUC ↓ 25% and C_{min} ↓ 44%	The effects of increases in progestin (norgestimate) are not fully known and may include insulin resistance, dyslipidemia, acne, and venous thrombosis. Decreased ethinyl estradiol may lead to more intermenstrual bleeding. Weigh the risks and benefits of using the drug and consider using an alternative ARV or contraceptive method.
		↑ drospirenone possible	Clinical monitoring is recommended due to the potential for hyperkalemia. Consider using alternative ARV or contraceptive method.
		↑ levonorgestrel possible ↑ norethindrone expected	No dose adjustment needed
Subdermal Implant Contraceptives (e.g., etonogestrel, levonorgestrel)	BIC, CAB (PO and IM), DTG, RAL	Etonogestrel ↑ 27% with DTG ↔ etonogestrel or levonorgestrel expected with BIC, CAB, RAL	No dose adjustment needed
	EVG/c	↑ etonogestrel expected ↑ levonorgestrel expected	No dose adjustment needed
Transdermal Contraceptives (e.g., ethinyl estradiol/ norelgestromin, ethinyl estradiol/ levonorgestrel)	BIC, CAB (PO, IM), DTG, RAL	↔ contraceptive expected	No dose adjustment needed
	EVG/c	↑ progestin possible ↓ ethinyl estradiol possible	No dose adjustment needed
Vaginal Ring Contraceptives (e.g., etonogestrel/ ethinyl estradiol, segesterone/ethinyl estradiol)	BIC, CAB (PO, IM), DTG, RAL	↔ contraceptive expected	No dose adjustment needed
	EVG/c	↑ progestin possible ↓ ethinyl estradiol possible	For segesterone/ethinyl estradiol vaginal rings, use alternative ARV or contraceptive methods.
Emergency Contraceptives **Levonorgestrel (PO)**	BIC, CAB (PO, IM), DTG, RAL	↔ levonorgestrel expected	No dose adjustment needed
	EVG/c	↑ levonorgestrel possible	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hormonal Therapies—Miscellaneous			
Menopausal Replacement Therapy	BIC, CAB (PO and IM), DTG, RAL	↔ estrogen expected with estradiol or conjugated estrogen (equine and synthetic) ↔ drospirenone, MPA, and micronized progesterone expected	No dose adjustment needed
	EVG/c	↓ or ↑ estrogen possible ↑ drospirenone possible ↑ oral MPA possible ↑ oral micronized progesterone possible	Adjust estrogen and progestin dose as needed based on clinical effects.
Miscellaneous	BIC, CAB (PO and IM), DTG, EVG/c, RAL	↔ goserelin, leuprolide acetate, and spironolactone expected	No dose adjustment needed
	BIC, CAB (PO and IM), DTG, RAL	↔ estrogen expected	No dose adjustment needed
		↔ testosterone expected	No dose adjustment needed
	EVG/c	↑ or ↓ estradiol possible ↑ cyproterone, dutasteride, and finasteride possible	Adjust dutasteride dose as needed based on clinical effects.
		↑ testosterone possible	Monitor effects of testosterone and monitor for adverse effects. Adjust testosterone dose as necessary.
Immunosuppressants			
Cyclosporine, Everolimus, Sirolimus, Tacrolimus	BIC, CAB (PO and IM), DTG, RAL	↔ immunosuppressant expected	No dose adjustment needed
	EVG/c	↑ immunosuppressant possible	Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant. Monitor for immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with a specialist as necessary.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lipid-Modifying			
Atorvastatin	BIC, CAB (PO and IM), DTG, RAL	↔ atorvastatin expected	No dose adjustment needed
	EVG/c	Atorvastatin AUC ↑ 2.6-fold and C_{max} ↑ 2.3-fold	Administer the lowest effective dose while monitoring for adverse events. Do not exceed 20 mg atorvastatin daily.
Fluvastatin	BIC, CAB (PO and IM), DTG, RAL	↔ fluvastatin expected	No dose adjustment needed
	EVG/c	↑ fluvastatin possible	Administer the lowest effective fluvastatin dose while monitoring for adverse events.
Lomitapide	BIC, CAB (PO and IM), DTG, RAL	↔ lomitapide expected	No dose adjustment needed
	EVG/c	↑ lomitapide expected	**Contraindicated**
Lovastatin	BIC, CAB (PO and IM), DTG, RAL	↔ lovastatin expected	No dose adjustment needed
	EVG/c	Significant ↑ lovastatin expected	**Contraindicated**
Pitavastatin, Pravastatin	BIC, CAB (PO and IM), DTG, RAL	↔ statin expected	No dose adjustment needed
	EVG/c	No data	No dose adjustment needed. Monitor for adverse events.
Rosuvastatin	BIC, CAB (PO and IM), DTG, RAL	↔ rosuvastatin expected	No dose adjustment needed
	EVG/c	Rosuvastatin AUC ↑ 38% and C_{max} ↑ 89%	Administer the lowest effective dose while monitoring for adverse events.
Simvastatin	BIC, CAB (PO and IM), DTG, RAL	↔ simvastatin expected	No dose adjustment needed
	EVG/c	Significant ↑ simvastatin expected	**Contraindicated**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Narcotics and Treatment for Opioid Dependence			
Buprenorphine Sublingual, buccal, or implant	BIC, CAB (PO and IM), DTG	↔ buprenorphine and norbuprenorphine (active metabolite) expected	No dose adjustment needed
	EVG/c	Buprenorphine AUC ↑ 35% and C_{min} ↑ 66% Norbuprenorphine (active metabolite) AUC ↑ 42% and C_{min} ↑ 57%	No dose adjustment needed. Monitor for adverse events of buprenorphine. When transferring buprenorphine from transmucosal administration to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.
	RAL	↔ buprenorphine and norbuprenorphine (active metabolite) (sublingual) ↔ buprenorphine or norbuprenorphine (active metabolite) expected (implant)	No dose adjustment needed
Fentanyl	BIC, CAB (PO and IM), DTG, RAL	↔ fentanyl expected	No dose adjustment needed
	EVG/c	↑ fentanyl	Monitor for fentanyl efficacy and adverse events, including potentially fatal respiratory depression.
Lofexidine	BIC, CAB (PO and IM), DTG, RAL	↔ lofexidine expected	No dose adjustment needed
	EVG/c	↑ lofexidine possible	Monitor for lofexidine-related adverse events, including symptoms of orthostasis and bradycardia.
Methadone	All INSTIs	↔ methadone	No dose adjustment needed
Tramadol	BIC, CAB (PO and IM), DTG, RAL	↔ tramadol and M1 (active metabolite) expected	No dose adjustment needed
	EVG/c	↑ tramadol expected ↓ M1 (active metabolite) possible	Tramadol dose adjustments may be necessary. Monitor for clinical response and tramadol-related adverse events.
PDE5 Inhibitors			
Avanafil	BIC, CAB (PO and IM), DTG, RAL	↔ avanafil expected	No dose adjustment needed
	EVG/c	No data	**Do not coadminister.**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Sildenafil	BIC, CAB (PO and IM), DTG, RAL	↔ sildenafil expected	No dose adjustment needed
	EVG/c	↑ sildenafil expected	**For Treatment of Erectile Dysfunction** • Start with sildenafil 25 mg every 48 hours and monitor for sildenafil-related adverse events. **Contraindicated** for treatment of PAH.
Tadalafil	BIC, CAB (PO and IM), DTG, RAL	↔ tadalafil expected	No dose adjustment needed
	EVG/c	↑ tadalafil expected	**For Treatment of Erectile Dysfunction** • Start with tadalafil 5 mg. Do not exceed a single dose of tadalafil 10 mg every 72 hours. Monitor for tadalafil-related adverse events. **For Treatment of PAH** *In Patients on EVG/c >7 Days* • Start with tadalafil 20 mg once daily. Increase to tadalafil 40 mg once daily based on tolerability. *In Patients on Tadalafil who Require EVG/c* • Stop tadalafil ≥24 hours before EVG/c initiation. Seven days after EVG/c initiation, restart tadalafil at 20 mg once daily and increase to tadalafil 40 mg once daily based on tolerability.
Vardenafil	BIC, CAB (PO and IM), DTG, RAL	↔ vardenafil expected	No dose adjustment needed
	EVG/c	↑ vardenafil expected	Start with vardenafil 2.5 mg every 72 hours and monitor for vardenafil-related adverse events.
Sedative/Hypnotics			
Benzodiazepines			
Alprazolam, Clonazepam, Clorazepate, Diazepam, Estazolam, Flurazepam	BIC, CAB (PO and IM), DTG, RAL	↔ benzodiazepine expected	No dose adjustment needed
	EVG/c	↑ benzodiazepine possible	Dose reduction of benzodiazepine may be necessary. Initiate with a low dose and monitor for benzodiazepine-related adverse events. Consider using an alternative benzodiazepine, such as lorazepam, oxazepam, or temazepam.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Midazolam, Triazolam	BIC, CAB (PO and IM), RAL	↔ benzodiazepine expected	No dose adjustment needed
	DTG	**With DTG 25 mg** • ↔ midazolam AUC	No dose adjustment needed
	EVG/c	↑ midazolam expected ↑ triazolam expected	**Contraindicated** **Do not coadminister** triazolam or oral midazolam and EVG/c. Parenteral midazolam can be administered in a closely monitored setting. Consider dose reduction, especially if >1 dose is administered.
Orexin Receptor Antagonists			
Daridorexant, Lemborexant, Suvorexant	BIC, CAB (PO and IM), DTG, RAL	↔ daridorexant, lemborexant, suvorexant expected	No dose adjustment needed
	EVG/c	↑ daridorexant, lemborexant, suvorexant expected	**Do not coadminister.**
Other Sedatives			
Eszopiclone	BIC, CAB (PO and IM), DTG, RAL	↔ eszopiclone expected	No dose adjustment needed
	EVG/c	↑ eszopiclone expected	Start with lowest dose and increase to a max of 2 mg daily. Monitor for eszopiclone-related adverse events.
Zolpidem	BIC, CAB (PO and IM), DTG, RAL	↔ zolpidem expected	No dose adjustment needed
	EVG/c	↑ zolpidem expected	Initiate zolpidem at a low dose. Dose reduction of zolpidem may be necessary.
Miscellaneous Drugs			
Calcifediol	BIC, CAB (PO and IM), DTG, RAL	↔ calcifediol expected	No dose adjustment needed
	EVG/c	↑ calcifediol possible	Dose adjustment of calcifediol may be required. Monitor serum 25-hydroxyvitamin D, intact PTH, and serum Ca concentrations.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cisapride	BIC, CAB (PO and IM), DTG, RAL	↔ cisapride expected	No dose adjustment needed
	EVG/c	↑ cisapride expected	**Contraindicated**
Colchicine	BIC, CAB (PO and IM), DTG, RAL	↔ colchicine expected	No dose adjustment needed
	EVG/c	↑ colchicine expected	**Do not coadminister** in patients with hepatic or renal impairment. **For Treatment of Gout Flares** • Administer a single dose of colchicine 0.6 mg, followed by colchicine 0.3 mg 1 hour later. Do not repeat dose for at least 3 days. **For Prophylaxis of Gout Flares** • If original dose was colchicine 0.6 mg twice daily, decrease to colchicine 0.3 mg once daily. If dose was 0.6 mg once daily, decrease to 0.3 mg every other day. **For Treatment of Familial Mediterranean Fever** • Do not exceed colchicine 0.6 mg once daily or 0.3 mg twice daily.
Dronabinol	BIC, CAB (PO and IM), DTG, RAL	↔ dronabinol expected	No dose adjustment needed
	EVG/c	↑ dronabinol possible	Monitor for dronabinol-related adverse events.
Eluxadoline	BIC, CAB (PO and IM), DTG, RAL	↔ eluxadoline expected	No dose adjustment needed
	EVG/c	↑ eluxadoline possible	Monitor for eluxadoline-related adverse events.
Ergot Derivatives	BIC, CAB (PO and IM), DTG, RAL	↔ dihydroergotamine, ergotamine, and methylergonovine expected	No dose adjustment needed
	EVG/c	↑ dihydroergotamine, ergotamine, and methylergonovine expected	**Contraindicated**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Finerenone	BIC, CAB (PO and IM), DTG, RAL	↔ finerenone expected	No dose adjustment needed
	EVG/c	↑ finerenone expected	**Contraindicated**
Flibanserin	BIC, CAB (PO and IM), DTG, RAL	↔ flibanserin expected	No dose adjustment needed
	EVG/c	↑ flibanserin expected	**Contraindicated**
Naloxegol	BIC, CAB (PO and IM), DTG, RAL	↔ naloxegol expected	No dosage adjustment needed
	EVG/c	↑ naloxegol expected	**Contraindicated**
Polyvalent Cation Supplements Mg, Al, Fe, Ca, Zn, including multivitamins with minerals. **Note:** Please refer to the Acid Reducers section in this table for recommendations on use with Al-, Mg-, and Ca-containing antacids.	BIC	↔ BIC AUC if administered simultaneously with Fe or Ca and food BIC AUC ↓ 33% if administered simultaneously with $CaCO_3$ under fasting conditions BIC AUC ↓ 63% if administered simultaneously with Fe under fasting conditions	**With Supplements That Contain Ca or Fe** • Administer BIC and supplements that contain Ca or Fe together with food. **Do not coadminister** BIC under fasting conditions simultaneously with, or 2 hours after, supplements that contain Ca or Fe.
	CAB	↓ INSTI possible	If coadministration is necessary, administer INSTI at least 2 hours before or at least 4 hours after supplements that contain polyvalent cations, including but not limited to the following products: cation-containing laxatives; Fe, Ca, or Mg supplements; and sucralfate. Monitor for virologic response. Many oral multivitamins also contain varying amounts of polyvalent cations; the extent and significance of chelation is unknown.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	DTG	DTG AUC ↓ 39% if administered simultaneously with $CaCO_3$ under fasting conditions DTG AUC ↓ 54% if administered simultaneously with Fe under fasting conditions ↔ DTG when administered with Ca or Fe supplement simultaneously with food	**With Supplements That Contain Ca or Fe** • Administer DTG and supplements that contain Ca or Fe together with food, or administer DTG at least 2 hours before or at least 6 hours after supplement. **Do not coadminister** DTG under fasting conditions simultaneously with, or 2 hours after, supplements that contain Ca or Fe.
	EVG/c, RAL	↓ INSTI possible	If coadministration is necessary, administer INSTI at least 2 hours before or at least 6 hours after supplements that contain polyvalent cations, including but not limited to the following products: cation-containing laxatives; Fe, Ca, or Mg supplements; and sucralfate. Monitor for virologic response. Many oral multivitamins also contain varying amounts of polyvalent cations; the extent and significance of chelation is unknown.
Praziquantel	BIC, CAB (PO and IM), DTG, RAL	↔ praziquantel and INSTI expected	No dose adjustment needed
	EVG/c	↑ praziquantel possible	Consider alternative ARV. If coadministration is necessary, monitor for praziquantel-related adverse events.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: Al = aluminum; ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; AST = aspartate aminotransferase; AUC = area under the curve; BIC = bictegravir; Ca = calcium; CAB = cabotegravir; $CaCO_3$ = calcium carbonate; CCB = calcium channel blocker; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; CMV = cytomegalovirus; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P450; DTG = dolutegravir; DVT = deep vein thrombosis; ECG = electrocardiogram; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; Fe = iron; FTC = emtricitabine; GI = gastrointestinal; IM = intramuscular; INR = international normalized ratio; INSTI = integrase strand transfer inhibitor; Mg = magnesium; MPA = medroxyprogesterone acetate; PAH = pulmonary arterial hypertension; PDE5 = phosphodiesterase type 5; PE = pulmonary embolism; PO = orally; PTH = parathyroid hormone; QTc = QT corrected for heart rate; RAL = raltegravir; RPV = rilpivirine; SSRI = selective serotonin reuptake inhibitors; TAF = tenofovir alafenamide; TCA = tricyclic antidepressants; TDF = tenofovir disoproxil fumarate; Zn = zinc

Table 24e. Drug Interactions Between the CCR5 Antagonist Maraviroc and Other Drugs (Including Antiretroviral Agents)

Updated: September 12, 2024
Reviewed: September 12, 2024

In the table below, "no dose adjustment needed" indicates that the U.S. Food and Drug Administration–approved dose of maraviroc (MVC) 300 mg twice daily should be used. Recommendations for managing a particular drug interaction may differ, depending on whether a new antiretroviral (ARV) drug is being initiated in a patient on a stable concomitant medication or a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgment to select the most appropriate alternative medication.

Concomitant Drug Class/ Name	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antibacterials—Macrolides		
Azithromycin	↔ MVC expected	No dose adjustment needed
Clarithromycin	↑ MVC possible	MVC 150 mg twice daily
Erythromycin	↑ MVC possible	No dose adjustment needed
Antifungals		
Fluconazole	↑ MVC possible	No dose adjustment needed
Isavuconazole	↑ MVC possible	No dose adjustment needed
Itraconazole	↑ MVC possible	MVC 150 mg twice daily
Posaconazole	↑ MVC possible	MVC 150 mg twice daily
Voriconazole	↑ MVC possible	MVC 150 mg twice daily
Antimycobacterials		
Rifabutin	MVC AUC ↔ and C_{min} ↓ 30%	**If Used *Without* a Strong CYP3A Inhibitor** • MVC 300 mg twice daily **If Used *With* a Strong CYP3A Inhibitor** • MVC 150 mg twice daily
Rifampin	MVC AUC ↓ 63%	**If Used *Without* a Strong CYP3A Inhibitor** • MVC 600 mg twice daily **If Used *With* a Strong CYP3A Inhibitor** • Consider alternative ARV or antimycobacterial
Rifapentine	**Rifapentine Weekly and Daily** ↓ MVC expected	Do not coadminister.

Table 24e. Drug Interactions Between the CCR5 Antagonist Maraviroc and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antiretroviral Drugs		
Attachment Inhibitor		
FTR[a]	MVC AUC ↑ 25% ↔ TMR[a]	No dose adjustment needed
Capsid Inhibitor		
LEN (SQ and PO)	↑ MVC possible	No dose adjustment needed
INSTIs		
BIC, CAB (IM and PO), DTG	↔ MVC expected	No dose adjustment needed
EVG/c	↑ MVC possible	MVC 150 mg twice daily.
RAL	MVC AUC ↓ 21% RAL AUC ↓ 37%	No dose adjustment needed
NNRTIs		
DOR, RPV (IM and PO)	↔ MVC expected	No dose adjustment needed
EFV	MVC AUC ↓ 45%	**If Used *Without* a Strong CYP3A Inhibitor** • MVC 600 mg twice daily **If Used *With* a Strong CYP3A Inhibitor** • MVC 150 mg twice daily
ETR	MVC AUC ↓ 53%	**If Used *Without* a Strong CYP3A Inhibitor** • MVC 600 mg twice daily **If Used *With* a Strong CYP3A Inhibitor** • MVC 150 mg twice daily
PIs		
ATV/c, ATV/r	**With (ATV/r 300 mg/100 mg) Once Daily** • MVC AUC ↑ 388%	MVC 150 mg twice daily
DRV/c, DRV/r	**With (DRV/r 600 mg/100 mg) Twice Daily** • MVC AUC ↑ 305% **With (DRV/r 600 mg/100 mg) Twice Daily and ETR** • MVC AUC ↑ 210%	MVC 150 mg twice daily

Table 24e. Drug Interactions Between the CCR5 Antagonist Maraviroc and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antiseizure		
Carbamazepine, Phenobarbital, Phenytoin	↓ MVC possible	**If Used *Without* a Strong CYP3A Inhibitor** • MVC 600 mg twice daily **If Used *With* a Strong CYP3A Inhibitor** • MVC 150 mg twice daily
Eslicarbazepine	↓ MVC possible	Consider alternative ARV or anticonvulsant.
Oxcarbazepine	↓ MVC possible	Consider alternative ARV or anticonvulsant.
Antivirals—Hepatitis C Direct-Acting Antivirals		
Elbasvir/Grazoprevir	↔ MVC expected	No dose adjustment needed
Ledipasvir/Sofosbuvir	↔ MVC expected	No dose adjustment needed
Glecaprevir/Pibrentasvir	↔ MVC expected	No dose adjustment needed
Simeprevir	↔ MVC expected	No dose adjustment needed
Sofosbuvir	↔ MVC expected	No dose adjustment needed
Sofosbuvir/Velpatasvir	↔ MVC expected	No dose adjustment needed
Sofosbuvir/Velpatasvir/Voxilaprevir	↔ MVC expected	No dose adjustment needed
Antivirals—Miscellaneous (e.g., for CMV, Mpox)		
Brincidofovir	↔ MVC expected	No dose adjustment needed
Cidofovir	↔ MVC expected	No dose adjustment needed
Tecovirimat	**When Given With MVC Without a Boosted PI or Other Potent CYP3A4 Inhibitors** • ↓ MVC possible but not expected to be clinically relevant **When Given With MVC Plus a Boosted PI or Other Potent CYP3A4 Inhibitors** • ↑ MVC expected	**If Used *Without* a Strong CYP3A Inhibitor** • No dose adjustment needed **If Used *With* a Strong CYP3A Inhibitor** • MVC 150 mg twice daily

Table 24e. Drug Interactions Between the CCR5 Antagonist Maraviroc and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antivirals—SARS-CoV-2		
Molnupiravir	↔ MVC expected	No dose adjustment needed
Remdesivir	↔ MVC expected	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	**MVC With Ritonavir 100 mg Twice Daily** • MVC AUC ↑ 161%	MVC 150 mg twice daily
Herbal Products		
St. John's Wort	↓ MVC expected	**Do not coadminister.**
Hormonal Therapies		
Hormonal Contraceptives	↔ ethinyl estradiol or levonorgestrel	No dose adjustment needed
Menopausal Hormone Replacement Therapy	↔ MVC or hormone replacement therapies expected	No dose adjustment needed

[a] FTR is a prodrug metabolized to its active moiety, TMR. Therefore, the effect on gp120-directed attachment inhibitor in the table refers to TMR concentrations.

Key to Symbols

↑ = increase
↓ = decrease
↔ = no change

Key: ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; CAB = cabotegravir; C_{min} = minimum plasma concentration; CMV = cytomegalovirus; CYP = cytochrome P; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FTR = fostemsavir; IM = intramuscular; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; ; PI = protease inhibitor; PO = orally; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQ = subcutaneous; TMR = temsavir

Table 24f. Drug Interactions Between HIV-1 gp120-Directed Attachment Inhibitors and Other Drugs (Including Antiretroviral Agents)

Updated: September 12, 2024
Reviewed: September 12, 2024

Fostemsavir (FTR), an HIV-1 gp120-directed attachment inhibitor, is a prodrug of temsavir (TMR). In this table, the effect on gp120-directed attachment inhibitor refers to TMR concentrations. Recommendations for managing a particular drug interaction may differ depending on whether a new antiretroviral (ARV) drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. Providers should exercise their clinical judgment to select the most appropriate alternative medication to use in cases where an interacting drug needs to be replaced with an alternative.

Concomitant Drug Class/ Name	Effect on gp120-Directed Attachment Inhibitor and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers		
H2 Receptor Antagonists	↔ TMR	No dose adjustment needed
Antibacterials—Antimycobacterials		
Rifabutin	**With Rifabutin 300 mg Once Daily and Without RTV** • TMR AUC ↓ 30% **With Rifabutin 150 mg Once Daily and With RTV 100 mg Once Daily** • TMR AUC ↑ 66%	**If Used *Without* PI/r** • No dose adjustment needed **If Used *With* PI/r** • Recommended dose is rifabutin 150 mg once daily. • No dose adjustment of FTR
Rifampin	TMR AUC ↓ 82%	**Contraindicated**
Rifapentine	**Daily and Weekly Dosing** ↓ TMR expected	**Do not coadminister.**
Antiretroviral Drugs		
Capsid Inhibitor		
LEN (SQ and PO)	↔ TMR expected ↔ LEN expected	No dose adjustment needed

Table 24f. Drug Interactions Between HIV-1 gp120-Directed Attachment Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on gp120-Directed Attachment Inhibitor and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
CCR5 Antagonist		
MVC	↔ TMR MVC AUC ↑ 25%	No dose adjustment needed
CD4 Post-Attachment Inhibitor		
IBA	↔ expected	No dose adjustment needed
INSTIs		
BIC, CAB (IM and PO), DTG, EVG/c	↔ TMR expected	No dose adjustment needed
RAL plus TDF	↔ TMR	No dose adjustment needed
NRTIs		
TDF	↔ TMR ↔ TDF	No dose adjustment needed
NNRTIs		
DOR, RPV (IM and PO)	↔ TMR expected	No dose adjustment needed
EFV	↓ TMR possible ↔ EFV expected	No dose adjustment needed
ETR	TMR AUC ↓ 50% ↔ ETR	No dose adjustment needed
ETR plus DRV/r	TMR C_{max} and AUC ↑ 34% to 53% ↔ DRV, RTV ETR AUC ↑ 28%	No dose adjustment needed

Table 24f. Drug Interactions Between HIV-1 gp120-Directed Attachment Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on gp120-Directed Attachment Inhibitor and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
PIs		
ATV/c	↑ TMR expected ↔ ATV expected	No dose adjustment needed
ATV/r	TMR C_{max} and AUC ↑ 54% to 58% ↔ ATV, RTV	No dose adjustment needed
DRV/c	TMR C_{max} and AUC ↑ 79% to 97% ↔ DRV, RTV expected	No dose adjustment needed
DRV/r	TMR C_{max} and AUC ↑ 52% to 63% ↔ DRV, RTV	No dose adjustment needed
Antiseizure		
Carbamazepine, Phenobarbital, Phenytoin	↓ TMR expected	**Contraindicated**
Antivirals—Hepatitis C Direct-Acting Antivirals		
Elbasvir/Grazoprevir	↑ grazoprevir expected	Increased grazoprevir exposures may increase the risk of ALT elevations. **Use an alternative** HCV regimen.
Ledipasvir/Sofosbuvir	↔ expected	No dose adjustment needed
Glecaprevir/Pibrentasvir	↔ expected	No dose adjustment needed
Sofosbuvir	↔ expected	No dose adjustment needed
Sofosbuvir/Velpatasvir	↔ expected	No dose adjustment needed
Sofosbuvir/Velpatasvir/Voxilaprevir	↑ voxilaprevir expected	**Use an alternative** HCV regimen if possible.
Antivirals—Miscellaneous (e.g., for CMV, Mpox)		
Brincidofovir	↑ brincidofovir possible	Give FTR dose at least 3 hours after administering brincidofovir, and monitor for brincidofovir-related adverse events (i.e., elevations in ALT/AST and bilirubin and GI adverse events).

Table 24f. Drug Interactions Between HIV-1 gp120-Directed Attachment Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on gp120-Directed Attachment Inhibitor and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cidofovir	↔ TMR expected	No dose adjustment needed
Tecovirimat	↔ TMR expected	No dose adjustment needed
Antivirals—SARS-CoV-2		
Molnupiravir	↔ expected	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	TMR AUC ↑ 45%	No dose adjustment needed
Remdesivir	↔ expected	No dose adjustment needed
Herbal Products		
St. John's Wort	↓ TMR expected	**Contraindicated**
Hormonal Therapies		
Hormonal Contraceptives	Ethinyl estradiol AUC ↑ 40% ↔ norethindrone	Prescribe oral contraceptive that contains no more than 30 mcg of ethinyl estradiol[a] or use alternative ARV or contraceptive methods.
Menopausal Hormone Replacement Therapy (e.g., conjugated estrogens, drospirenone, estradiol, medroxyprogesterone, progesterone)	↑ estrogens, estradiol possible	Use lowest effective dose for estrogen-containing regimens.
Lipid-Modifying Agents		
Atorvastatin, Fluvastatin, Pitavastatin, Simvastatin	↑ statin possible ↔ expected	Increased statin concentration may not be clinically relevant. Follow clinical guidelines. Administer the lowest effective statin dose while monitoring for adverse events.
Rosuvastatin	Rosuvastatin AUC ↑ 69%	Increased rosuvastatin concentration may not be clinically relevant. Follow clinical guidelines. Administer the lowest effective dose while monitoring for adverse events.

Table 24f. Drug Interactions Between HIV-1 gp120-Directed Attachment Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on gp120-Directed Attachment Inhibitor and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Narcotics and Treatment for Opioid Dependence		
Buprenorphine/Naloxone	Buprenorphine AUC ↑ 30% Norbuprenorphine (active metabolite) AUC ↑ 39%	No dose adjustment needed
Methadone	↔ Total methadone ↔ R(−) methadone (active metabolite) ↔ S(+) methadone	No dose adjustment needed

[a] The following products contain no more than 30 mcg of ethinyl estradiol combined with norethindrone or norgestimate: Lo Minastrin Fe; Lo Loestrin Fe; Loestrin 1/20, 1.5/30; Loestrin Fe 1/20, 1.5/30; Loestrin 24 Fe; Minastrin 24 Fe; Ortho Tri-Cyclen Lo. Generic formulations also may be available.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: ALT = alanine aminotransferase; ARV = antiretroviral; AST = aspartate aminotransferase; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; C_{max} = maximum plasma concentration; CAB = cabotegravir; CCR5 = C-C chemokine receptor type 5; CMV = cytomegalovirus; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FTR = fostemsavir; GI = gastrointestinal; gp120 = glycoprotein 120; HCV = hepatitis C virus; IBA = ibalizumab; IM = intramuscular; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/r = ritonavir-boosted PI; PO = orally; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQ = subcutaneous; TDF = tenofovir disoproxil fumarate; TMR = temsavir

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Updated: September 12, 2024
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This table provides information on the known or predicted interactions between lenacapavir (LEN), an HIV capsid inhibitor, and other drugs, including antiretroviral (ARV) drugs.

LEN is available as an oral tablet (to be used only as initial therapy) and a long-acting injectable formulation that is administered every 6 months. LEN is a moderate cytochrome P450 (CYP) 3A4 inhibitor and may increase the concentration of drugs metabolized by CYP3A4. Due to the long half-life of the injectable formulation, this inhibitory effect may persist, and clinicians should continue to assess for drug interactions for up to 9 months after the last LEN injection. Recommendations for managing a particular drug interaction may differ depending on whether LEN is being initiated in a patient on a stable concomitant medication or whether a new medication is being initiated in a patient on a stable LEN-containing ARV regimen.

The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. Providers should exercise their clinical judgment to select the most appropriate alternative medication to use in cases where an interacting drug needs to be replaced with an alternative. People with HIV should be counseled about the importance of informing all their health care providers about their HIV regimen prior to starting any new concomitant medications (e.g., prescription, over-the-counter, and herbal or dietary supplements) to minimize the risk of drug–drug interactions.

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers		
Antacids, H2 Receptor Antagonists, Proton Pump Inhibitors	↔ expected	No dose adjustment needed
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia		
Alfuzosin	↑ alfuzosin expected	Consider an alternative to alfuzosin or an alternative ARV. If coadministered, monitor blood pressure.
Doxazosin	↑ doxazosin possible	No dose adjustment needed. Monitor blood pressure.
Tamsulosin	↑ tamsulosin possible	Initiate tamsulosin at 0.4 mg/day. Monitor blood pressure.
Terazosin	↔ expected	No dose adjustment needed
Silodosin	↑ silodosin possible	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antibacterials—Antimycobacterials		
Bedaquiline	↑ bedaquiline expected	Consider alternatives unless benefits outweigh risks. Monitor liver function and ECG for QTc prolongation.
Rifabutin	↓ LEN expected	**Do not coadminister.**
Rifampin	LEN AUC ↓ 84%	**Contraindicated**
Rifapentine	**Daily and Weekly Dosing** • ↓ LEN expected	**Do not coadminister.**
Antibacterials—Macrolides		
Azithromycin	↔ expected	No dose adjustment needed
Clarithromycin	↑ LEN possible	No dose adjustment needed
Erythromycin	↑ LEN possible	No dose adjustment needed
Anticoagulants		
Apixaban	↑ apixaban possible	No dose adjustment needed Monitor for apixaban-related adverse events, such as increased bleeding.
Dabigatran	↑ dabigatran possible	No dose adjustment needed Monitor for dabigatran-related adverse events, such as increased bleeding.
Edoxaban	↑ edoxaban possible	No dose adjustment needed Monitor for edoxaban-related adverse events, such as increased bleeding.
Rivaroxaban	↑ rivaroxaban possible	Monitor for rivaroxaban-related adverse events, such as increased bleeding, and adjust rivaroxaban dose accordingly.
Warfarin	↑ warfarin possible	Monitor INR and adjust warfarin dose accordingly.

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antidepressants, Anxiolytics, and Antipsychotics Also see the Sedative/Hypnotics section below.		
Bupropion	↔ expected	No dose adjustment needed
Buspirone	↑ buspirone expected	Administer lowest dose of buspirone with caution and titrate buspirone dose based on clinical response. Dose reduction may be necessary. Monitor for buspirone-related adverse events.
Desvenlafaxine	↔ expected	No dose adjustment needed
Duloxetine	↔ expected	No dose adjustment needed
Mirtazapine	↑ mirtazapine possible	No dose adjustment needed. Monitor for mirtazapine-related adverse events.
Nefazodone	↑ LEN possible	No dose adjustment needed
Selective Serotonin Reuptake Inhibitor (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, vortioxetine)	↑ paroxetine possible ↔ citalopram, escitalopram, fluoxetine, fluvoxamine, sertraline, vortioxetine expected	Dose reduction may be necessary with paroxetine. No dose adjustment needed
Trazodone	↑ trazodone expected	Administer lowest dose of trazodone and monitor for CNS and CV adverse events.
Tricyclic Antidepressants (e.g., amitriptyline, doxepin, nortriptyline)	↔ expected	No dose adjustment needed
Venlafaxine	↔ expected	No dose adjustment needed
Antipsychotics		
Aripiprazole	↑ aripiprazole possible	No dose adjustment needed
Brexpiprazole	↑ brexpiprazole expected	If patient is a known CYP2D6 poor metabolizer, then administer one-quarter of usual brexpiprazole dose.
Cariprazine	↑ cariprazine possible	No dose adjustment needed
Iloperidone	↑ iloperidone possible	No dose adjustment needed or consider dose reduction. Monitor for iloperidone-related adverse events.

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lumateperone	↑ lumateperone expected	Reduce dose of lumateperone to 21 mg once daily.
Lurasidone	↑ lurasidone expected	If LEN is added to lurasidone therapy, administer half of lurasidone dose. If lurasidone is added to LEN therapy, the recommended starting dose of lurasidone is 20 mg daily, and the maximum recommended dose is 80 mg daily.
Olanzapine **Olanzapine/Samidorphan**	↔ LEN olanzapine expected ↑ samidorphan possible	No dose adjustment needed
Other Antipsychotics (e.g., clozapine, risperidone, thioridazine)	↑ clozapine possible	No dose adjustment needed. Monitor for clozapine-related adverse events.
	↑ risperidone possible	No dose adjustment needed
	↑ thioridazine possible ↓ LEN possible	**Do not coadminister.**
Pimavanserin	↑ pimavanserin possible	No dose adjustment needed. Monitor ECG for QTc prolongation.
Pimozide	↑ pimozide expected	**Contraindicated**
Quetiapine	↑ quetiapine expected	Consider alternatives unless benefits outweigh risks. Monitor ECG for QTc prolongation and consider dose reduction accordingly.
Ziprasidone	↔ expected	No dose adjustment needed
Antifungals		
Fluconazole	↑ LEN possible	No dose adjustment needed
Ibrexafungerp	↑ ibrexafungerp possible	No dose adjustment needed
Isavuconazole	↔ expected	No dose adjustment needed
Itraconazole	↑ LEN possible	No dose adjustment needed
Posaconazole	↑ LEN possible	No dose adjustment needed
Voriconazole	↑ LEN AUC 41%	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antimalarials		
Artemether/Lumefantrine	↑ artemether and lumefantrine possible	Monitor for lumefantrine-related adverse events, including QTc prolongation.
Artesunate	↔ expected	No dose adjustment needed
Atovaquone/Proguanil	↔ expected	No dose adjustment needed
Mefloquine	↑ mefloquine possible	Monitor for mefloquine-related adverse events, including QTc prolongation.
Antimigraine		
Ergot Derivatives	↑ dihydroergotamine, ergotamine, and methylergonovine expected	**Do not coadminister.**
Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists		
Atogepant	↑ atogepant expected	No dose adjustment needed
Rimegepant	↑ rimegepant expected	Avoid a second dose of rimegepant within 48 hours.
Ubrogepant	↑ ubrogepant expected	Avoid a second dose of ubrogepant within 24 hours.
Zavegepant	↔ expected	No dose adjustment needed
Serotonin 5-HT1B, 1D Receptor Agonist		
Almotriptan	↔ expected	No dose adjustment needed
Eletriptan	↑ eletriptan expected	No dose adjustment needed. Monitor for eletriptan-related adverse events.
Frovatriptan, Naratriptan, Rizatriptan, Sumatriptan, Zolmitriptan	↔ expected	No dose adjustment needed
Antiplatelets		
Clopidogrel	↓ clopidogrel active metabolite possible	Consider alternative ARV or antiplatelet drug. If coadministered, monitor for clopidogrel-related adverse events.
Prasugrel	↔ expected	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Ticagrelor	↑ ticagrelor possible	No dose adjustment needed. Monitor for ticagrelor-related adverse events.
Vorapaxar	↑ vorapaxar possible	No dose adjustment needed
Antipneumocystis and Antitoxoplasmosis		
Atovaquone Oral suspension	↔ expected	No dose adjustment needed
Antiretroviral Drugs		
CCR5 Antagonist		
MVC	↔ expected	No dose adjustment needed
CD4 Post-attachment Inhibitor		
IBA	↔ expected	No dose adjustment needed
gp120 Attachment Inhibitor		
FTR	↔ expected	No dose adjustment needed
INSTIs		
BIC, CAB (IM or PO), DTG, EVG/c, RAL	↔ expected	No dose adjustment needed
NRTIs		
ABC, 3TC, FTC	↔ expected	No dose adjustment needed
TAF	TAF AUC ↑ 32%	No dose adjustment needed
TDF	TDF AUC ↑ 47%	No dose adjustment needed
NNRTIs		
EFV	LEN AUC↓ 56%	**Do not coadminister.**
ETR	↓ LEN expected	**Do not coadminister.**
DOR	↑ DOR possible	No dose adjustment needed
RPV (IM or PO)	↑ RPV possible	No dose adjustment needed
PIs		
ATV/r	↑ LEN expected	**Do not coadminister.**
ATV/c	LEN AUC ↑ 4-fold	**Do not coadminister.**
DRV/c	DRV/c AUC ↑ 94%	No dose adjustment needed
DRV/r	↑ LEN expected	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antiseizure		
Carbamazepine	↓ LEN expected	**Contraindicated**
Eslicarbazepine	↓ LEN expected	**Do not coadminister.**
Ethosuximide	↑ ethosuximide possible	Monitor for ethosuximide-related adverse events and adjust ethosuximide dose accordingly.
Lamotrigine	↔ expected	No dose adjustment needed
Oxcarbazepine	↓ LEN expected	**Do not coadminister.**
Phenobarbital	↓ LEN expected	**Do not coadminister.**
Phenytoin	↓ LEN expected	**Contraindicated**
Primidone	↓ LEN expected	**Do not coadminister.**
Valproic Acid	↔ expected	No dose adjustment needed
Antivirals—Hepatitis C		
Elbasvir/Grazoprevir	↔ expected	No dose adjustment needed
Glecaprevir/Pibrentasvir	↔ expected	No dose adjustment needed
Ledipasvir/Sofosbuvir	↔ expected	No dose adjustment needed
Sofosbuvir/Velpatasvir	↔ expected	No dose adjustment needed
Sofosbuvir/Velpatasvir/Voxilaprevir	↔ expected	No dose adjustment needed
Antivirals—Miscellaneous (e.g., for CMV, Mpox)		
Brincidofovir	↔ expected	No dose adjustment needed
Cidofovir	↔ expected	No dose adjustment needed
Maribavir	↔ expected	No dose adjustment needed
Tecovirimat	↓ LEN possible	No dose adjustment needed
Valganciclovir	↔ expected	No dose adjustment needed
Antivirals—SARS-CoV-2		
Molnupiravir	↔ expected	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	↑ LEN possible	No dose adjustment needed
Remdesivir	↔ expected	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Beta-Agonists, Long-Acting Inhaled		
Arformoterol, Formoterol, Indacaterol, Olodaterol, Salmeterol	↔ expected	No dose adjustment needed
Cardiac Medications		
Antiarrhythmics		
Amiodarone	↑ amiodarone expected ↑ LEN possible	**Do not coadminister.**
Digoxin	↑ digoxin expected	Consider alternative ARV or antiarrhythmic. If coadministered, monitor digoxin therapeutic concentration.
Disopyramide	↑ disopyramide expected	**Do not coadminister.**
Dofetilide	↔ expected	No dose adjustment needed
Dronedarone	↑ dronedarone possible ↑ LEN possible	Consider alternative ARV or cardiac medication. If coadministered, monitor for dronedarone-related adverse events.
Flecainide	↔ expected	No dose adjustment needed
Lidocaine	↑ propafenone possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor for antiarrhythmic-related adverse events and monitor concentrations, if available.
Mexiletine	↔ expected	No dose adjustment needed
Propafenone	↑ propafenone possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor for antiarrhythmic-related adverse events and monitor concentrations, if available.
Quinidine	↑ quinidine expected	**Do not coadminister.**
Sotalol	↔ expected	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Beta-Blockers		
Atenolol, Bisoprolol, Carvedilol, Labetalol, Metoprolol, Nebivolol, Timolol	↔ expected	No dose adjustment needed
Calcium Channel Blockers		
Amlodipine, Felodipine, Nifedipine	↑ amlodipine, felodipine expected ↑ nifedipine possible	Monitor and dose adjust according to clinical response and adverse events.
Diltiazem, Verapamil	↑ diltiazem possible ↔ verapamil expected	No dose adjustment needed
Cardiac – Other		
Bosentan	↓ LEN expected	**Do not coadminister.**
Eplerenone	↑ eplerenone expected	**For Post-MI CHF** • Dosing of eplerenone should not exceed 25 mg daily. **For Hypertension** • Initiate at 25 mg once daily. Dosing may be increased to a maximum of 25 mg twice daily.
Ivabradine	↑ ivabradine expected	**Do not coadminister.**
Mavacamten	↓ LEN possible ↑ mavacamten expected	Initiate mavacamten at the recommended starting dose of 5 mg daily in patients who are on stable therapy with LEN. Reduce dose of mavacamten by one level (i.e., 15 to 10 mg, 10 to 5 mg, or 5 to 2.5 mg) in patients who are on mavacamten treatment and intend to initiate LEN.
Ranolazine	↑ ranolazine expected	Limit ranolazine to 500 mg twice daily.
Corticosteroids		
Beclomethasone Inhaled or intranasal **Ciclesonide** Inhaled	↔ expected	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Budesonide, Fluticasone, Mometasone Inhaled or intranasal	↑ glucocorticoids possible	Initiate with the lowest starting dose and titrate carefully and monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-related adverse events.
Betamethasone Systemic	↑ betamethasone possible ↓ LEN possible	**Do not coadminister.**
Budesonide, Prednisone, Prednisolone Systemic	↑ glucocorticoids expected	Initiate with the lowest starting dose, titrate carefully, and monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-related adverse events.
Dexamethasone Systemic	↑ dexamethasone expected ↓ LEN expected if used with dexamethasone >16 mg/day	Initiate with the lowest starting dose, titrate carefully, and monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-related adverse events. **Do not coadminister** with dexamethasone >16 mg/day**.**
Betamethasone, Methylprednisolone, Triamcinolone Local injections, including intra-articular, epidural, or intra-orbital	↑ glucocorticoids possible	Monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-related adverse events.
Glucose-Lowering		
Canagliflozin	↔ expected	No dose adjustment needed
Saxagliptin	↑ saxagliptin possible	No dose adjustment needed
Dapagliflozin/Saxagliptin	↑ saxagliptin possible	No dose adjustment needed
Herbal Products		
St. John's Wort	↓ LEN expected	**Contraindicated**
Hormonal Therapies—Contraceptives		
Injectable Contraceptives Depot MPA	↑ MPA possible	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Oral Contraceptives (e.g., desogestrel, drospirenone, ethinyl estradiol, levonorgestrel, norgestimate)	↑ contraceptive exposures possible	No dose adjustment needed
Subdermal Implant Contraceptives (e.g., etonogestrel, levonorgestrel)	↑ contraceptive exposures possible	No dose adjustment needed
Transdermal Contraceptives (e.g., ethinyl estradiol/norelgestromin, ethinyl estradiol/levonorgestrel)	↑ contraceptive exposures possible	No dose adjustment needed
Vaginal Ring Contraceptives (e.g., etonogestrel/ethinyl estradiol, segesterone/ethinyl estradiol)	↑ contraceptive exposures possible	No dose adjustment needed
Emergency Contraceptives Levonorgestrel (oral)	↑ levonorgestrel possible	No dose adjustment needed
Hormonal Therapies—Miscellaneous		
5-Alpha Reductase Inhibitors (e.g., dutasteride, finasteride)	↑ dutasteride and finasteride possible	No dose adjustment needed
Estradiol	↔ expected	No dose adjustment needed
Goserelin, Leuprolide Acetate	↔ expected	No dose adjustment needed
Menopausal Hormone Replacement Therapy (e.g., conjugated estrogens, drospirenone, estradiol, medroxyprogesterone, progesterone)	↑ estrogen and progesterone possible ↑ drospirenone possible	No dose adjustment needed
Testosterone	↑ testosterone possible	No dose adjustment needed
Immunosuppressants		
Cyclosporine, Everolimus, Sirolimus, Tacrolimus	↑ immunosuppressant expected	Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant and monitor for immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with a specialist as necessary.

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lipid-Modifying		
Atorvastatin	↑ atorvastatin possible	No dose adjustment needed
Fluvastatin	↔ expected	No dose adjustment needed
Lomitapide	↑ lomitapide expected	**Contraindicated**
Lovastatin	↑ lovastatin expected	Administer the lowest effective lovastatin dose while monitoring for adverse events.
Pitavastatin	↔ expected	No dose adjustment needed
Pravastatin	↔ expected	No dose adjustment needed
Rosuvastatin	↑ rosuvastatin possible	No dose adjustment needed
Simvastatin	↑ simvastatin expected	Administer the lowest effective simvastatin dose while monitoring for adverse events.
Narcotics and Treatment for Opioid Dependence		
Buprenorphine Sublingual, buccal, or implant	↑ buprenorphine possible	**Initiation of Buprenorphine in Patients Taking LEN** • Titrate buprenorphine dose to desired effect and use the lowest feasible initial dose. **Initiation of LEN in Patients Taking Buprenorphine** • Dose adjustment for buprenorphine may be needed. Monitor for buprenorphine-related adverse events.
Fentanyl	↑ fentanyl possible	Monitor for fentanyl-related adverse events, including potentially fatal respiratory depression. Fentanyl dose reduction may be necessary.
Lofexidine	↔ expected	No dose adjustment needed
Methadone	↑ methadone possible	**Initiation of Methadone in Patients Taking LEN** • Titrate methadone dose to desired effect and use the lowest feasible initial dose.

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		Initiation of LEN in Patients Taking Methadone • Dose adjustment for methadone may be needed. Monitor for buprenorphine-related adverse events.
Oxycodone	↑ oxycodone possible	Monitor for opioid-related adverse events, including potentially fatal respiratory depression. Oxycodone dose reduction may be necessary.
Tramadol	↑ tramadol possible	Tramadol dose adjustments may be necessary. Monitor for clinical response and tramadol-related adverse events.
PDE5 Inhibitors		
Avanafil	↑ avanafil expected	Avanafil dose should not exceed 50 mg once every 24 hours.
Sildenafil	↑ sildenafil expected	**For Treatment of Erectile Dysfunction** • Start with sildenafil 25 mg and monitor for sildenafil-related adverse events. **For Treatment of PAH** • Reduce the dose of sildenafil to 20 mg three times a day when discontinuing treatment with LEN.
Tadalafil	↑ tadalafil expected	**For Treatment of Erectile Dysfunction** • For once-daily use: Consider maximum dose of 2.5 mg daily. If higher dose is needed, consider alternative PDE5 inhibitor. • For use as needed: Consider maximum dose of 10 mg every 72 hours. If higher dosing is needed, consider alternative PDE5 inhibitor. **For Treatment of PAH** • **Do not coadminister.**

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		For Treatment of Benign Prostatic Hyperplasia • Consider maximum dose of 2.5 mg daily. Use caution and monitor for AEs if dose increases to 5 mg.
Vardenafil	↑ vardenafil expected	Vardenafil dose should not exceed 5 mg once every 24 hours.
Sedative/Hypnotics		
Benzodiazepines		
Alprazolam, Diazepam, Triazolam	↑ benzodiazepine expected	Consider lowest dose and monitor for benzodiazepine-related adverse events.
Clonazepam	↑ clonazepam possible	Use with caution and consider alternative benzodiazepines.
Lorazepam, Oxazepam, Temazepam	↔ expected	No dose adjustment needed
Midazolam (Oral)	↑ midazolam AUC 259–308%	Use with caution and consider alternative benzodiazepine.
Orexin Receptor Antagonist		
Daridorexant, Lemborexant, Suvorexant	↑ daridorexant expected ↑ lemborexant expected ↑ suvorexant expected	Maximum recommended daridorexant dose is 25 mg. **Do not coadminister** with lemborexant. Initiate suvorexant dose at 5 mg daily. Suvorexant dose can be increased to 10 mg once per night if the 5 mg dose is not effective. **Do not exceed** 10 mg per night.
Other Sedatives		
Eszopiclone	↑ eszopiclone expected	Consider lowest dose and monitor for eszopiclone-related adverse events.
Zolpidem	↑ zolpidem possible	Consider initiating zolpidem at a low dose.
Miscellaneous Drugs		
Calcifediol	↑ calcifediol possible	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cisapride	↑ cisapride expected	**Do not coadminister.**
Colchicine	↑ colchicine expected	**For Treatment of Gout Flares** • Administer single colchicine dose of 1.2 mg. Do not repeat dose for at least 3 days. **For Treatment of Familial Mediterranean Fever** • Colchicine dose should not exceed 1.2 mg daily (may be given as 0.6 mg twice a day).
Dronabinol	↔ expected	No dose adjustment needed
Eluxadoline	↔ expected	No dose adjustment needed
Finerenone	↑ finerenone expected	Monitor serum potassium at initiation and during therapy according to finerenone product labeling.
Flibanserin	↑ flibanserin expected	**Contraindicated**
Naloxegol	↑ naloxegol expected	Avoid use; if coadministration is necessary, decrease dosage of naloxegol and monitor for naloxegol-related adverse events.
Praziquantel	↑ praziquantel possible	Consider alternative antiretroviral. If coadministration is necessary, monitor for praziquantel-related adverse events.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: 3TC = lamivudine; ABC = abacavir; AE = adverse event; AUC = area under the curve; ARV = antiretroviral; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CAB = cabotegravir; CD4 = CD4 T lymphocyte; CHF = congestive heart failure; CMV = cytomegalovirus; CNS = central nervous system; CV = cardiovascular; CYP = cytochrome P450; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; ECG = electrocardiogram; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; FTR = fostemsavir; IBA = ibalizumab; IM = intramuscular; INR = international normalized ratio; INSTI = integrase strand transfer inhibitor; QTc = QT corrected for heart rate; LEN = lenacapavir; MI = myocardial infarction; MPA = medroxyprogesterone acetate; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PAH = pulmonary arterial hypertension; PDE5 = phosphodiesterase type 5; PI = protease inhibitor; PO = orally; RAL = raltegravir; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Table 25a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors

Updated: September 12, 2024
Reviewed: September 12, 2024

Note: Interactions associated with unboosted atazanavir (ATV), delavirdine (DLV), fosamprenavir (FPV), indinavir (IDV), lopinavir (LPV), nelfinavir (NFV), nevirapine (NVP), saquinavir (SQV), and tipranavir (TPV) are **not** included in this table. Please refer to the U.S. Food and Drug Administration product labels for information regarding interactions between these drugs and other concomitant drugs.

Rilpivirine (RPV) intramuscular (IM) is not included in this table, because the combination of cabotegravir (CAB) IM plus RPV IM is a two-drug co-packaged product. Therefore, RPV IM is not expected to be used with a protease inhibitor.

PIs		NNRTIs			
		DOR	**EFV**	**ETR**	**RPV**
ATV/c	**PK Data**	↑ DOR expected ↔ ATV expected	↔ EFV expected ↓ ATV possible ↓ COBI possible	↑ ETR possible ↓ ATV possible ↓ COBI possible	↑ RPV PO possible ↔ ATV expected
	Dose	No dose adjustment needed	**ATV/c in ART-Naive Patients** • ATV 400 mg plus COBI 150 mg once daily • **Do not use** coformulated ATV 300 mg/COBI 150 mg. **ATV/c in ART-Experienced Patients** • **Do not coadminister.** No dose adjustment needed for EFV.	**Do not coadminister.**	No dose adjustment needed

Table 25a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors

PIs		NNRTIs			
		DOR	**EFV**	**ETR**	**RPV**
ATV/r	**PK Data**	↑ DOR expected ↔ ATV expected	↔ EFV expected **(ATV 400 mg Plus RTV 100 mg) Once Daily** • ATV concentrations similar to (ATV 300 mg plus RTV 100 mg) without EFV	**(ATV 300 mg Plus RTV 100 mg) Once Daily** • ETR AUC and C_{min} both ↑ ~30% • ↔ ATV AUC and C_{min}	↑ RPV PO possible ↔ ATV expected
	Dose	No dose adjustment needed	**ATV/r in ART-Naive Patients** • (ATV 400 mg plus RTV 100 mg) once daily **ATV/r in ART-Experienced Patients** • **Do not coadminister.** No dose adjustment needed for EFV	No dose adjustment needed	No dose adjustment needed
DRV/c	**PK Data**	↑ DOR expected ↔ DRV expected	↔ EFV expected ↓ DRV possible ↓ COBI possible	**ETR 400 mg Once Daily With (DRV 800 mg Plus COBI 150 mg) Once Daily** • ↔ ETR AUC and C_{min} • ↔ DRV AUC and C_{min} ↓ 56% • COBI AUC ↓ 30% and C_{min} ↓ 66%	↔ DRV expected ↑ RPV PO possible
	Dose	No dose adjustment needed	**Do not coadminister.**	**Do not coadminister.**	No dose adjustment needed

Table 25a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors

PIs		NNRTIs			
		DOR	**EFV**	**ETR**	**RPV**
DRV/r	**PK Data**	↑ DOR expected ↔ DRV expected	**With (DRV 300 mg Plus RTV 100 mg) Twice Daily** • EFV AUC ↑ 21% • ↔ DRV AUC and C_{min} ↓ 31%	**ETR 100 mg Twice Daily With (DRV 600 mg Plus RTV 100 mg) Twice Daily** • ETR AUC ↓ 37% and C_{min} ↓ 49% • ↔ DRV	**RPV 150 mg PO Once Daily With (DRV 800 mg Plus RTV 100 mg) Once Daily** • RPV PO AUC ↑ 130% and C_{min} ↑ 178% • ↔ DRV
	Dose	No dose adjustment needed	Clinical significance unknown. Use standard doses and monitor patient closely. Consider monitoring drug levels.	No dose adjustment needed Despite reduced ETR concentration, safety and efficacy of this combination have been established in a clinical trial.	No dose adjustment needed

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: ART = antiretroviral therapy; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{min} = minimum plasma concentration; COBI = cobicistat; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; EFV = efavirenz; ETR = etravirine; NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PO = oral; PK = pharmacokinetic; RPV = rilpivirine; RTV = ritonavir

Table 25b. Interactions Between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors

Updated: September 12, 2024
Reviewed: September 12, 2024

Recommendations for managing a particular drug interaction may differ depending on whether a new antiretroviral (ARV) drug is being initiated in a patient on a stable concomitant medication, or a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly.

Information on drug interactions with oral (PO) cabotegravir (CAB) is not included in this table. The CAB PO tablet is not available in retail pharmacies and will be provided directly to people with HIV for short-term use only (PO lead-in and to bridge if intramuscular [IM] administration is delayed).

CAB IM and rilpivirine (RPV) IM are not included in this table because the combination is a two-drug, co-packaged product. Therefore, it is not anticipated that they will be used with PO non-nucleoside reverse transcriptase inhibitors (NNRTIs) or protease inhibitors (PIs).

ARV Drugs by Drug Class		INSTIs			
		BIC	**DTG**	**EVG/c**	**RAL**
NNRTIs					
DOR	**PK Data**	↔ DOR and BIC expected	↔ DOR DTG AUC ↑ 36% and C_{min} ↑ 27%	↑ DOR expected ↔ EVG	↔ DOR and RAL expected
	Dose	No dose adjustment needed.	No dose adjustment needed.	No dose adjustment needed.	No dose adjustment needed.
EFV	**PK Data**	↓ BIC expected	**With DTG 50 mg Once Daily** • DTG AUC ↓ 57% and C_{min} ↓ 75%	↑ or ↓ EVG, COBI, and EFV possible	**With RAL 400 mg Twice Daily** • RAL AUC ↓ 36% and C_{min} ↓ 21% **With RAL 1,200 mg Once Daily** • ↔ RAL AUC and C_{min}

Table 25b. Interactions Between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors

ARV Drugs by Drug Class		INSTIs			
		BIC	**DTG**	**EVG/c**	**RAL**
	Dose	**Do not coadminister.**	**In Patients Without INSTI Resistance** • DTG 50 mg twice daily **In Patients With Certain INSTI-Associated Resistance[a] or Clinically Suspected INSTI Resistance** • Consider alternative combination	**Do not coadminister.**	No dose adjustment needed.
ETR	**PK Data**	↓ BIC expected	**ETR 200 mg Twice Daily Plus DTG 50 mg Once Daily** • DTG AUC ↓ 71% and C_{min} ↓ 88% **ETR 200 mg Twice Daily With (DRV 600 mg Plus RTV 100 mg) Twice Daily and DTG 50 mg Once Daily** • DTG AUC ↓ 25% and C_{min} ↓ 37%	↑ or ↓ EVG, COBI, and ETR possible	**ETR 200 mg Twice Daily Plus RAL 400 mg Twice Daily** • ETR C_{min} ↑ 17% • RAL C_{min} ↓ 34%
	Dose	**Do not coadminister.**	**Do not coadminister** ETR and DTG without concurrently administering ATV/r or DRV/r. **In Patients Without INSTI Resistance** • DTG 50 mg once daily with ETR (concurrently with ATV/r or DRV/r)	**Do not coadminister.**	RAL 400 mg twice daily Coadministration with RAL 1,200 mg once daily **is not recommended.**

Table 25b. Interactions Between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors

ARV Drugs by Drug Class		INSTIs			
		BIC	**DTG**	**EVG/c**	**RAL**
			In Patients With Certain INSTI-Associated Resistance[a] or Clinically Suspected INSTI Resistance • DTG 50 mg twice daily with ETR (concurrently with ATV/r or DRV/r)		
RPV	**PK Data**	No data	**With DTG 50 mg Once Daily** • ↔ DTG AUC and C_{min} ↑ 22% • ↔ RPV PO AUC and C_{min} ↑ 21%	↑ RPV PO possible	↔ RPV PO RAL C_{min} ↑ 27%
	Dose	No dose adjustment needed.	No dose adjustment needed.	**Do not coadminister.**	No dose adjustment needed.
PIs					
ATV/c	**PK Data**	BIC AUC ↑ 306%	No data	Not applicable	No data
	Dose	**Do not coadminister.**	No dose adjustment needed.	**Do not coadminister** two COBI-containing products.	No dose adjustment needed.
ATV/r	**PK Data**	↑ BIC expected	**(ATV 300 mg Plus RTV 100 mg) Once Daily Plus DTG 30 mg Once Daily** • DTG AUC ↑ 62% and C_{min} ↑ 121%	Not applicable	**With (ATV 300 mg Plus RTV 100 mg) Once Daily** • RAL AUC ↑ 41%
	Dose	**Do not coadminister.**	No dose adjustment needed.	Do not coadminister RTV and COBI.	No dose adjustment needed.

Table 25b. Interactions Between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors

ARV Drugs by Drug Class		INSTIs			
		BIC	**DTG**	**EVG/c**	**RAL**
DRV	**PK Data**	Not applicable	Not applicable	↔ DRV or EVG expected	Not applicable
	Dose	**Do not administer** DRV without RTV or COBI.	**Do not administer** DRV without RTV or COBI.	No dose adjustment needed.	**Do not administer** DRV without RTV or COBI.
DRV/c	**PK Data**	BIC AUC ↑ 74%	**DRV/c Plus DTG Once Daily** • ↔ DTG, DRV, and COBI **DTG 50 mg Once Daily and DRV/r Once Daily Switched to DRV/c** • DTG C_{min} ↑ 100%	Not applicable	No data
	Dose	No dose adjustment needed.	No dose adjustment needed.	**Do not coadminister** two COBI-containing products.	No dose adjustment needed.
DRV/r	**PK Data**	No data	**(DRV 600 mg Plus RTV 100 mg) Twice Daily With DTG 30 mg Once Daily** • DTG AUC ↓ 22% and C_{min} ↓ 38%	Not applicable	**With (DRV 600 mg Plus RTV 100 mg) Twice Daily** • RAL AUC ↓ 29% and Cmin ↑ 38%
	Dose	No dose adjustment needed.	No dose adjustment needed.	**Do not coadminister** RTV and COBI.	No dose adjustment needed.

[a] Refer to DTG product label for details.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: ARV = antiretroviral; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; C_{min} = minimum plasma concentration; COBI = cobicistat; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; INSTI = integrase strand transfer inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PK = pharmacokinetic; PO = oral; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir