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

Updated: June 3, 2021
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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 (ARV) drugs. EVG is always coadministered with cobicistat. 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 INSTIs and other 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 judgement to select the most appropriate alternative medication to use.

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.

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Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	CAB IM	↔ CAB IM expected	No dose adjustment needed.
	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.

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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 and adverse events. 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 for tamsulosin-related adverse events.
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 and adverse events. 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			
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.
	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.

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Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	RAL	RAL AUC ↑ 19% 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.
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%	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. Do not coadminister DTG with once-daily rifapentine.

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Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	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.
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%	Dabigatran dosing recommendation depends on indication and renal function. Refer to dabigatran prescribing information for dosing instructions when using dabigatran concomitantly with P-glycoprotein inhibitors.

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Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
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. Deep Venous Thrombosis and Pulmonary Embolism • 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.
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.
Anticonvulsants			
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.

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Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
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.
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	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	All INSTIs	No data	Monitor valproic acid concentration and virologic response.
Antidepressants, Anxiolytics, and Antipsychotics Also see the Sedative/Hypnotics section below			
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.
Nefazodone	BIC, CAB (PO and IM), DTG, RAL	↔ nefazodone expected	No dose adjustment needed.
	EVG/c	↑ nefazodone expected	Consider alternative ARV or antidepressant.
Trazodone	BIC, CAB (PO and IM), DTG, RAL	↔ trazodone expected	No dose adjustment needed.

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Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Tricyclic Antidepressants 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 Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline	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.
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 efficacy 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.
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 efficacy 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.

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Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	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.
Olanzapine	All INSTIs	↔ olanzapine expected	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.

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Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
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			
Isavuconazole	BIC, CAB (PO and IM), DTG, RAL	↑ INSTI possible	No dose adjustment needed.
	EVG/c	↑ isavuconazole expected ↑ or ↓ EVG and COBI possible	If coadministered, consider monitoring isavuconazole concentrations and assessing virologic response.
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.

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	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.
Antihyperglycemics			
Metformin	BIC	Metformin AUC ↑ 39%	Monitor for adverse events of metformin.
	DTG	DTG 50 mg Once Daily plus Metformin 500 mg Twice Daily • Metformin AUC ↑ 79% and C_{max} ↑ 66% DTG 50 mg Twice Daily plus Metformin 500 mg Twice Daily • Metformin AUC ↑ 2.4-fold and C_{max} ↑ 2-fold	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.
	CAB (PO and IM), RAL	↔ metformin expected	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.
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.

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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.
Antivirals—Orthopoxviruses (Smallpox, 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 (i.e., elevations in ALT/AST and bilirubin and GI adverse events).
Cidofovir	BIC, CAB (PO and IM), DTG, 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.
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.

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	EVG/c	↑ salmeterol possible	Do not coadminister due to the potential for increased risk of salmeterol-associated cardiovascular events.
Cardiac Medications			
Amiodarone	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ amiodarone expected	No dose adjustment needed.
	EVG/c	↑ INSTI possible ↑ amiodarone possible	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.
Bepridil, Digoxin, Disopyramide, Dronedarone, Flecainide, Systemic Lidocaine, Mexilitine, Propafenone, Quinidine	BIC, CAB (PO and IM), DTG	↔ expected for the listed antiarrhythmics, except for disopyramide ↑ disopyramide possible	No dose adjustment needed. Monitor for disopyramide-related adverse events.
	RAL	↔ expected for the listed antiarrhythmics	No dose adjustment needed.
	EVG/c	↑ antiarrhythmics possible Digoxin C_{max} ↑ 41% and ↔ AUC	Therapeutic drug monitoring for antiarrhythmics, if available, is recommended.
Beta Blockers (e.g., metoprolol, timolol)	BIC, CAB (PO and IM), DTG, RAL	↔ beta blocker expected	No dose adjustment needed.
	EVG/c	↑ beta blocker possible	Beta blocker dose may need to be decreased; adjust dose based on clinical response. Consider using an alternative ARV or a beta blocker that is not metabolized by CYP450 enzymes (e.g., atenolol, labetalol, nadolol, sotalol).
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.

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Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Calcium Channel Blockers	BIC	↑ BIC possible with diltiazem ↔ expected for all other CCBs	No dose adjustment needed.
	CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ CCB expected	No dose adjustment needed.
	EVG/c	↑ CCB possible	Titrate CCB dose and monitor for CCB efficacy and adverse events.
Dofetilide	BIC, DTG	↑ dofetilide expected	Contraindicated.
	CAB (PO and IM), RAL	↔ dofetilide expected	No dose adjustment needed.
	EVG/c	↑ dofetilide possible	Do not coadminister.
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.
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.
	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.

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
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.
Hepatitis C Direct-Acting Antiviral Agents			
Daclatasvir	BIC, CAB (PO and IM), RAL	↔ daclatasvir expected	No dose adjustment needed.
	DTG	↔ daclatasvir	No dose adjustment needed.
	EVG/c	↑ daclatasvir	Decrease daclatasvir dose to 30 mg once daily.
Dasabuvir plus Ombitasvir/Paritaprevir/RTV	BIC	↔ BIC expected	No dose adjustment needed.
	CAB (PO and IM)	↔ CAB expected ↑ RPV IM expected	Do not coadminister due to potential for QTc prolongation with higher concentrations of RPV. RPV is co-packaged and coadministered with CAB IM.
	DTG	↔ DTG, dasabuvir, plus ombitasvir/paritaprevir/RTV	No dose adjustment needed.
	EVG/c	No data	Do not coadminister.
	RAL	RAL AUC ↑ 134%	No dose adjustment needed.
Elbasvir/Grazoprevir	BIC	↔ BIC expected	No dose adjustment needed.
	CAB (PO and IM)	↔ CAB, elbasvir, and grazoprevir 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 ↔ 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%	
	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	

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	↔ 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.
	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ sofosbuvir, velpatasvir, and voxilaprevir expected	No dose adjustment needed.
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			
Contraceptives: Non-Oral	BIC, CAB (PO and IM), DTG, RAL	Etonogestrel (subdermal implant) ↑ 27% with DTG ↔ expected with BIC, CAB, RAL	No dose adjustment needed.
	EVG/c	No data	No data available to make dose recommendation.
Contraceptives: Oral	BIC, DTG, RAL	↔ ethinyl estradiol and norgestimate ↔ INSTI	No dose adjustment needed.
	CAB (PO and IM)	↔ ethinyl estradiol and levonorgestrel with CAB PO	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	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.
Gender-Affirming Therapy	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	↑ estradiol possible ↑ cyproterone, dutasteride, and finasteride possible	Adjust dutasteride dose as needed based on clinical effects and endogenous hormone concentrations.
		↑ testosterone possible	Monitor masculinizing effects of testosterone and monitor for adverse effects. Adjust testosterone dose as necessary.
Menopausal Replacement Therapy	BIC, CAB (PO and IM), DTG, RAL	↔ estrogen expected with estradiol or conjugated estrogen (equine and synthetic) ↔ drospirenone, medroxyprogesterone, and micronized progesterone expected	No dose adjustment needed.
	EVG/c	↓ or ↑ estrogen possible ↑ drospirenone possible ↑ oral medroxyprogesterone possible ↑ oral micronized progesterone possible	Adjust estrogen and progestin dose as needed based on clinical effects.
Immunosuppressants			
Cyclosporine, Everolimus, Sirolimus, Tacrolimus	BIC, CAB (PO and IM), DTG, RAL	↔ immunosuppressant 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	↑ 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.
Lipid-Modifying Agents			
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	Titrate statin dose carefully. Administer the lowest effective dose while monitoring for adverse events. Do not exceed 20 mg atorvastatin daily.
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 data available for dose recommendation.
Rosuvastatin	BIC, CAB (PO and IM), DTG, RAL	↔ rosuvastatin expected	No dose adjustment needed.
	EVG/c	Rosuvastatin AUC ↑ 38% and C_{max} ↑ 89%	Titrate statin dose carefully and use 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.
Narcotics and Treatment for Opioid Dependence			
Buprenorphine	BIC, CAB (PO and IM), DTG	↔ buprenorphine and norbuprenorphine (active metabolite) 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
Sublingual, buccal, or implant	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.
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 adverse effects of sildenafil. Contraindicated for treatment of PAH.

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
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 adverse effects of tadalafil. 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 adverse effects of vardenafil.
Sedative/Hypnotics			
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.
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.

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
Suvorexant	BIC, CAB (PO and IM), DTG, RAL	↔ suvorexant expected	No dose adjustment needed.
	EVG/c	↑ suvorexant expected	Do not coadminister.
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.
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.

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
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.
Flibanserin	BIC, CAB (PO and IM), DTG, RAL	↔ flibanserin expected	No dose adjustment needed.
	EVG/c	↑ flibanserin 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.
	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.

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, 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.

Key to Symbols

↑ = increase
↓ = decrease
↔ = no change

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; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; DTG = dolutegravir; 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; PAH = pulmonary arterial hypertension; PDE5 = phosphodiesterase type 5; PO = orally; PTH = parathyroid hormone; QTc = QT corrected for heart rate; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SSRI = selective serotonin reuptake inhibitors; TAF = tenofovir alafenamide; TCA = tricyclic antidepressants; TDF = tenofovir disoproxil fumarate; Zn = zinc