



Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

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Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated July 14, 2016; last reviewed July 14, 2016) (page 1 of 11)

This table provides information on known or predicted pharmacokinetic interactions between INSTIs (DTG, EVG, or RAL) and non-ARV drugs. EVG is always coadministered with either COBI or RTV. In this table, the drug interactions with EVG/c products and those with EVG plus PI/r are presented separately. When EVG is given with a PI/r, clinicians should refer to [Table 19a](#) for recommendations on the management of drug interactions of concomitant medications and the specific PI/r used with EVG.

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Aluminium, Magnesium +/- Calcium-Containing Antacids Please refer to the Miscellaneous Drugs section of this table for recommendations on use with other polyvalent cation products (eg, iron, calcium supplements, multivitamins).	DTG	DTG AUC ↓ 74% if given simultaneously with antacid; DTG AUC ↓ 26% if given 2 hours before antacid	Give DTG at least 2 hours before or at least 6 hours after antacids containing polyvalent cations.
	EVG/c EVG plus PI/r	EVG AUC ↓ 40% to 50% if given simultaneously with antacid EVG AUC ↓ 15% to 20% if given 2 hours before or after antacid; ↔ with 4-hour interval	Separate EVG/c/TDF/FTC and antacid administration by more than 2 hours.
	RAL	<u>Al-Mg Hydroxide Antacid:</u> • RAL C _{min} ↓ 54% to 63% <u>CaCO₃ Antacid:</u> • RAL C _{min} ↓ 32%	Do not coadminister RAL and Al-Mg hydroxide antacids. Use alternative acid reducing agent. No dosing separation necessary when coadministering RAL and CaCO ₃ antacids.
H2-Receptor Antagonists	EVG/c	No significant effect	No dosage adjustment necessary.
	EVG plus PI/r	↔ EVG	No dosage adjustment necessary for EVG. Refer to Table 19a for information on PI/r interactions.
PPIs	DTG	No significant effect	No dosage adjustment necessary.
	EVG/c	No significant effect	No dosage adjustment necessary.
	EVG plus PI/r	↔ EVG	No dosage adjustment necessary for EVG. Refer to Table 19a for information on PI/r interactions.
	RAL	RAL AUC ↑ 212% and C _{min} ↑ 46%	No dosage adjustment necessary.
Anticoagulants and Antiplatelets			
Apixaban	EVG/c EVG plus PI/r	↑ apixaban expected	Avoid concomitant use.
Dabigatran	EVG/c EVG plus PI/r	↑ dabigatran possible	No dosage adjustment for dabigatran if CrCl >50 mL/min. Avoid coadministration if CrCl <50 mL/min.
Edoxaban	EVG/c EVG plus PI/r	↑ edoxaban expected	Avoid concomitant use.
Rivaroxaban	EVG/c EVG plus PI/r	↑ rivaroxaban expected	Avoid concomitant use.

Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated July 14, 2016; last reviewed July 14, 2016) (page 2 of 11)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anticoagulants and Antiplatelets, continued			
Ticagrelor	EVG/c EVG plus PI/r	↑ ticagrelor expected	Avoid concomitant use.
Vorapaxar	EVG/c EVG plus PI/r	↑ vorapaxar expected	Avoid concomitant use.
Warfarin	EVG/c EVG plus PI/r	Warfarin levels may be affected	Monitor INR and adjust warfarin dose accordingly.
Anticonvulsants			
Carbamazepine Phenobarbital Phenytoin	DTG	↓ DTG possible	Consider alternative anticonvulsant.
	EVG/c	carbamazepine AUC ↑ 43% EVG AUC ↓ 69% and C _{min} ↓ >99% ↓ COBI expected	Contraindicated. Do not coadminister.
	EVG plus PI/r	↓ EVG	Consider alternative anticonvulsant.
Ethosuximide	EVG/c EVG plus PI/r	↑ ethosuximide possible	Clinically monitor for ethosuximide toxicities.
Oxcarbazepine	DTG EVG/c EVG plus PI/r	↓ INSTI possible	Consider alternative anticonvulsant.
Antidepressants/Anxiolytics/Antipsychotics Also see Sedative/Hypnotics section below.			
Bupropion	EVG/c	↑ or ↓ bupropion possible	Titrate bupropion dose based on clinical response.
	EVG plus PI/r	↓ bupropion possible	Titrate bupropion dose based on clinical response.
Buspirone	EVG/c EVG plus PI/r	↑ buspirone possible	Initiate buspirone at a low dose. Dose reduction may be necessary.
Fluvoxamine	EVG/c EVG plus PI/r	↑ or ↓ EVG possible	Consider alternative antidepressant or ARV.
Quetiapine	EVG/c EVG plus PI/r	↑ quetiapine AUC expected.	<u>Initiation of quetiapine in a patient receiving EVG/c:</u> <ul style="list-style-type: none"> Start quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine efficacy and adverse effects. <u>Initiation of EVG/c in a patient receiving a stable dose of quetiapine:</u> <ul style="list-style-type: none"> Reduce quetiapine dose to 1/6 of the original dose, and closely monitor for quetiapine efficacy and adverse effects.

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Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antidepressants/Anxiolytics/Antipsychotics, continued Also see Sedative/Hypnotics section below.			
SSRIs Citalopram Escitalopram Fluoxetine Paroxetine Sertraline	EVG/c	↑ SSRI possible	Initiate with lowest dose of SSRI and titrate dose carefully based on antidepressant response.
	EVG plus PI/r	↑ or ↓ SSRI possible	Titrate SSRI dose based on clinical response.
	RAL	↔ RAL ↔ citalopram	No dosage adjustment necessary.
TCAs Amitriptyline Desipramine Doxepin Imipramine Nortriptyline	EVG/c	Desipramine AUC ↑ 65%	Initiate with lowest dose of TCA and titrate dose carefully.
	EVG plus PI/r	↑ TCA expected	Initiate with lowest dose of TCA and titrate dose carefully based on antidepressant response and/or drug levels.
Trazodone	EVG/c EVG plus PI/r	↑ trazodone possible	Initiate with lowest dose of trazodone and titrate dose carefully.
Antifungals			
Isavuconazole	EVG/c	↑ isavuconazole expected ↑ EVG and COBI possible	If coadministered, consider monitoring isavuconazole concentrations and assess virologic response.
	EVG plus PI/r	Changes in isavuconazole and EVG possible	Refer to Table 19a for PI recommendations.
Itraconazole	EVG/c	↑ itraconazole expected ↑ EVG and COBI possible	Consider monitoring itraconazole level to guide dosage adjustments. High itraconazole doses (>200 mg/day) are not recommended unless dose is guided by itraconazole levels.
	EVG plus PI/r	↑ EVG possible	Refer to Table 19a for PI recommendations.
Posaconazole	EVG/c	↑ EVG and COBI possible ↑ posaconazole possible	If coadministered, monitor posaconazole concentrations.
	EVG plus PI/r	↑ EVG possible	Refer to Table 19a for PI recommendations.
Voriconazole	EVG/c	↑ voriconazole expected ↑ EVG and COBI possible	Risk/benefit ratio should be assessed to justify use of voriconazole. If administered, consider monitoring voriconazole level. Adjust dose accordingly.
	EVG plus PI/r	Changes in voriconazole and EVG possible	Refer to Table 19a for PI recommendations.

Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated July 14, 2016; last reviewed July 14, 2016) (page 4 of 11)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antimycobacterials			
Clarithromycin	EVG/c	↑ clarithromycin possible ↑ COBI possible	<u>CrCl 50–60 mL/min:</u> • Reduce clarithromycin dose by 50%. <u>CrCl <50 mL/min:</u> • EVG/c is not recommended.
	DTG	<u>Rifabutin (300 mg once daily):</u> • DTG AUC ↔ and C _{min} ↓ 30%	No dosage adjustment necessary.
Rifabutin	EVG/c	<u>Rifabutin 150 mg every other day with EVG/c once daily compared to Rifabutin 300 mg once daily alone:</u> ↔ rifabutin AUC 25-O-desacetyl-rifabutin AUC ↑ 625% EVG AUC ↓ 21%, C _{min} ↓ 67%	Do not coadminister.
	EVG plus PI/r	↔ EVG ↔ rifabutin AUC 25-O-desacetyl-rifabutin AUC ↑ 951%	Refer to Table 19a for dosing recommendations for rifabutin with PI.
	RAL	RAL AUC ↑ 19% and C _{min} ↓ 20%	No dosage adjustment necessary.
	DTG	<u>Rifampin with DTG 50 mg BID compared to DTG 50 mg BID alone:</u> DTG AUC ↓ 54%, C _{min} ↓ 72% <u>Rifampin with DTG 50 mg BID compared to DTG 50 mg once daily alone:</u> DTG AUC ↑ 33%, C _{min} ↑ 22%	<u>Dose:</u> DTG 50 mg BID (instead of 50 mg once daily) for patients without suspected or documented INSTI mutation. Alternative to rifampin should be used in patients with certain suspected or documented INSTI-associated resistance substitutions. Consider using rifabutin.
Rifampin	EVG/c EVG plus PI/r	Significant ↓ EVG and COBI expected	Do not coadminister.
	RAL	<u>RAL 400 mg:</u> • RAL AUC ↓ 40%, C _{min} ↓ 61% <u>Compared with RAL 400 mg BID alone, Rifampin with RAL 800 mg BID:</u> • RAL AUC ↑ 27%, C _{min} ↓ 53%	<u>Dose:</u> • RAL 800 mg BID Monitor closely for virologic response or consider using rifabutin as an alternative rifamycin.
	DTG	Significant ↓ DTG expected	Do not coadminister.
Rifapentine	EVG/c EVG plus PI/r	Significant ↓ EVG and COBI expected	Do not coadminister.
	RAL	<u>Rifapentine 600 mg once daily:</u> RAL C _{min} ↓ 41%	Do not coadminister with once-daily rifapentine.
	RAL	<u>Rifapentine 900 mg once weekly:</u> RAL AUC ↑ 71%, C _{min} ↓ 12%	For once-weekly rifapentine, use standard doses.

Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated July 14, 2016; last reviewed July 14, 2016) (page 5 of 11)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cardiac Medications			
Antiarrhythmics Amiodarone Bepridil Digoxin Disopyramide Dronedarone Flecainide Systemic lidocaine Mexilitine Propafenone Quinidine	EVG/c	↑ antiarrhythmics possible digoxin C _{max} ↑ 41% and AUC no significant change	Use antiarrhythmics with caution. Therapeutic drug monitoring, if available, is recommended for antiarrhythmics.
	EVG plus PI/r	↑ antiarrhythmics possible	Refer to Table 18 and 19a for use of antiarrhythmics and PI/r.
Bosentan	EVG/c	↑ bosentan possible	<u>In patients on EVG/c ≥10 days:</u> • Start bosentan at 62.5 mg once daily or every other day based on individual tolerability. <u>In patients on bosentan who require EVG/c:</u> • 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.
	EVG plus PI/r	↑ bosentan possible	Refer to Table 19a for recommendations on bosentan dosing when used with PI/r.
Beta-blockers (eg, metoprolol, timolol)	EVG/c	↑ beta-blockers possible	Beta-blocker dose may need to be decreased; adjust dose based on clinical response. Consider using beta-blockers that are not metabolized by CYP450 enzymes (eg, atenolol, labetalol, nadolol, sotalol).
	EVG plus PI/r		
CCBs	EVG/c	↑ CCBs possible	Coadminister with caution. Titrate CCB dose and monitor for CCB efficacy and toxicities. Refer to Table 19a for diltiazem plus ATV/r and SQV/r recommendations.
	EVG plus PI/r		
Dofetilide	DTG	↑ dofetilide expected	Do not coadminister.
Eplerenone	EVG/c EVG plus PI/r	↑ eplerenone expected	Contraindicated. Do not coadminister.
Ivabradine	EVG/c EVG plus PI/r	↑ ivabradine expected	Contraindicated. Do not coadminister.

Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated July 14, 2016; last reviewed July 14, 2016) (page 6 of 11)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Corticosteroids			
Dexamethasone (systemic)	EVG/c	↓ EVG and COBI possible	Use systemic dexamethasone with caution. Monitor virologic response to ART. Consider alternative corticosteroid.
	EVG plus PI/r	↓ EVG possible	
Fluticasone Inhaled/Intranasal	EVG/c	↑ fluticasone possible	Coadministration may result in adrenal insufficiency and Cushing's syndrome. Consider alternative therapy (eg, beclomethasone), particularly for long-term use.
	EVG plus PI/r		
Methylprednisolone Prednisolone Triamcinolone Local injections, including intra-articular, epidural, intra-orbital	EVG/c	↑ glucocorticoids expected	Coadministration may result in adrenal insufficiency and Cushing's syndrome. Do not coadminister.
	EVG plus PI/r		
Hepatitis C Direct Acting Antivirals			
Daclatasvir	DTG	↔ Daclatasvir	No dosage adjustment necessary.
	EVG/c	↑ Daclatasvir	Decrease daclatasvir dose to 30 mg once daily.
	EVG plus PI/r	↑ Daclatasvir expected	Decrease daclatasvir dose to 30 mg once daily, regardless of which PI/r is used, except for TPV/r. Do not coadminister EVG plus TPV/r with daclatasvir.
	RAL	No data	No dosage adjustment necessary.
Dasabuvir plus Ombitasvir/Paritaprevir/r	DTG	No data	No dosing recommendations at this time.
	EVG plus PI/r	No data	Do not coadminister.
	EVG/c		
Elbasvir/Grazoprevir	RAL	RAL AUC ↑ 134%	No dosage adjustment necessary.
	DTG	↔ Elbasvir ↔ Grazoprevir ↔ DTG	No dosage adjustment necessary.
	EVG plus PI/r		Refer to Table 19a for PI dosing recommendations.
	EVG/c	↑ elbasvir, grazoprevir expected	Coadministration is not recommended.
Ledipasvir/Sofosbuvir	RAL	↔ Elbasvir ↔ Grazoprevir RAL ↔ with elbasvir RAL AUC ↑ 43% with grazoprevir	No dosage adjustment necessary.
	EVG/c	↑ TDF and ↑ ledipasvir expected	Do not coadminister.
	EVG/c	↔ EVG/c/TAF/FTC expected	No dosage adjustment necessary.
	EVG plus PI/r	↔ EVG expected	Refer to Table 19a for PI dosing recommendations.
Ledipasvir/Sofosbuvir	DTG	↔ DTG or RAL	No dosage adjustment necessary.
	RAL		

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Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hepatitis C Direct Acting Antivirals, continued			
Simeprevir	DTG	↔ DTG expected	No dosage adjustment necessary.
	EVG/c	↑ simeprevir expected	Coadministration is not recommended.
	EVG plus PI/r	↔ EVG expected	Coadministration is not recommended.
	RAL	No significant effect	No dosage adjustment necessary.
Sofosbuvir	All INSTIs	No significant effect expected	No dosage adjustment necessary.
Herbal Products			
St. John's Wort	DTG	↓ DTG possible	Do not coadminister.
	EVG/c	↓ EVG and COBI possible	Do not coadminister.
	EVG plus PI/r		
Hormonal Contraceptives			
Hormonal Contraceptives	RAL	No clinically significant effect	No dosage adjustment necessary.
Norgestimate/Ethinyl Estradiol	DTG	No significant effect	No dosage adjustment necessary.
	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 can include insulin resistance, dyslipidemia, acne, and venous thrombosis. Weigh the risks and benefits of the drug, and consider alternative contraceptive method.
	EVG plus PI/r	↔ EVG	Refer to Table 19a for recommendations when used with PI/r.
HMG-CoA Reductase Inhibitors			
Atorvastatin	EVG/c	↑ atorvastatin possible	Titrate statin dose slowly and use the lowest dose possible.
	EVG plus PI/r	↔ EVG expected	Refer to Table 19a for dosing recommendations when used with PI/r.
Lovastatin	EVG/c EVG plus PI/r	Significant ↑ lovastatin expected	Contraindicated. Do not coadminister.
Pitavastatin Pravastatin	EVG/c	No data	No dosage recommendation
	EVG plus PI/r	↔ EVG expected	Refer to Table 19a for dosing recommendations when used with PI/r.
Rosuvastatin	EVG/c	Rosuvastatin AUC ↑ 38% and C _{max} ↑ 89%	Titrate statin dose slowly and use the lowest dose possible.
	EVG plus PI/r	↔ EVG expected	Refer to Table 19a for dosing recommendations when used with PI/r.
Simvastatin	EVG/c EVG plus PI/r	Significant ↑ simvastatin expected	Contraindicated. Do not coadminister.

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Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Immunosuppressants			
Cyclosporine Everolimus Sirolimus Tacrolimus	EVG/c EVG plus PI/r	↑ immunosuppressant possible	Initiate with an adjusted immunosuppressant dose to account for potential increased concentration and monitor for toxicities. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.
Narcotics/Treatment for Opioid Dependence			
Buprenorphine Sublingual/Buccal/Implant	EVG/c	Buprenorphine AUC ↑ 35%, C _{max} ↑ 12%, and C _{min} ↑ 66% Norbuprenorphine AUC ↑ 42%, C _{max} ↑ 24%, and C _{min} ↑ 57%	No dosage adjustment necessary. Clinical monitoring is recommended. When transferring buprenorphine from transmucosal to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.
	EVG plus PI/r	↔ EVG expected	Refer to Table 19a for dosing recommendations when used with PI/r.
	RAL	No significant effect observed (sublingual) or expected (implant)	No dosage adjustment necessary.
Methadone	DTG	No significant effect	No dosage adjustment necessary.
	EVG/c	No significant effect	No dosage adjustment necessary.
	EVG plus PI/r	↓ methadone	Opioid withdrawal unlikely but may occur. Dosage adjustment of methadone is not usually required. Monitor for opioid withdrawal and increase methadone dose as clinically indicated.
	RAL	No significant effect	No dosage adjustment necessary.
Neuroleptics			
Perphenazine Risperidone Thioridazine	EVG/c	↑ neuroleptic possible	Initiate neuroleptic at a low dose. Decrease in neuroleptic dose may be necessary.
PDE5 Inhibitors			
Avanafil	EVG/c EVG plus PI/r	No data	Coadministration is not recommended.
Sildenafil	EVG/c EVG plus PI/r	↑ sildenafil expected	<u>For treatment of erectile dysfunction:</u> • Start with sildenafil 25 mg every 48 hours and monitor for adverse effects of sildenafil. <u>For treatment of PAH:</u> • Contraindicated

Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated July 14, 2016; last reviewed July 14, 2016) (page 9 of 11)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
PDE5 Inhibitors, continued			
Tadalafil	EVG/c EVG plus PI/r	↑ tadalafil expected	<p>For treatment of erectile dysfunction:</p> <ul style="list-style-type: none"> • Start with tadalafil 5-mg dose and do not exceed a single dose of 10 mg every 72 hours. Monitor for adverse effects of tadalafil. <p>For treatment of PAH</p> <p><i>In patients on EVG/c >7 days:</i></p> <ul style="list-style-type: none"> • Start with tadalafil 20 mg once daily and increase to 40 mg once daily based on tolerability. <p><i>In patients on tadalafil who require EVG/c:</i></p> <ul style="list-style-type: none"> • Stop tadalafil ≥24 hours before EVG/c initiation. Seven days after EVG/c initiation, restart tadalafil at 20 mg once daily, and increase to 40 mg once daily based on tolerability.
Vardenafil	EVG/c EVG plus PI/r	↑ vardenafil expected	Start with vardenafil 2.5 mg every 72 hours and monitor for adverse effects of vardenafil.
Sedative/Hypnotics			
Clonazepam Clorazepate Diazepam Estazolam Flurazepam	EVG/c EVG plus PI/r	↑ benzodiazepines possible	<p>Dose reduction of benzodiazepine may be necessary. Initiate with low dose and clinically monitor.</p> <p>Consider alternative benzodiazepines to diazepam, such as lorazepam, oxazepam, or temazepam.</p>
Midazolam Triazolam	DTG	<u>With DTG 25 mg:</u> midazolam AUC ↔	No dosage adjustment necessary.
	EVG/c EVG plus PI/r	↑ midazolam expected ↑ triazolam expected	<p>Do not coadminister triazolam or oral midazolam and EVG/c or (EVG plus PI).</p> <p>Parenteral midazolam can be used with caution in a closely monitored setting. Consider dose reduction, especially if more than one dose is administered.</p>
Suvorexant	EVG/c EVG plus PI/r	↑ suvorexant expected	Coadministration is not recommended.
Zolpidem	EVG/c EVG plus PI/r	↑ zolpidem expected	Initiate zolpidem at a low dose. Dose reduction may be necessary.

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Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Miscellaneous Drugs			
Colchicine	EVG/c EVG plus PI/r	↑ colchicine expected	Do not coadminister in patients with hepatic or renal impairment. <u>For treatment of gout flares:</u> • Colchicine 0.6 mg for 1 dose, followed by 0.3 mg 1 hour later. Do not repeat dose for at least 3 days. <u>For prophylaxis of gout flares:</u> • If original dose was colchicine 0.6 mg BID, decrease to colchicine 0.3 mg once daily. If regimen was 0.6 mg once daily, decrease to 0.3 mg every other day. <u>For treatment of familial Mediterranean fever:</u> • Do not exceed colchicine 0.6 mg once daily or 0.3 mg BID.
Flibanserin	EVG/c EVG plus PI/r	↑ flibanserin expected	Contraindicated. Do not coadminister.
Metformin	DTG	<u>DTG 50 mg once daily plus metformin 500 mg BID:</u> Metformin AUC ↑ 79%, C _{max} ↑ 66% <u>DTG 50 mg BID plus metformin 500 mg BID:</u> Metformin AUC ↑ 2.4 fold, C _{max} ↑ 2 fold	Limit metformin dose to no more than 1,000 mg per day. When starting/stopping DTG in patient on metformin, dose adjustment of metformin may be necessary to maintain optimal glycemic control and/or minimize GI symptoms.
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.	All INSTIs	↓ INSTI possible DTG ⇔ when administered with Ca or Fe supplement simultaneously with food	If coadministration is necessary, give INSTI at least 2 hours before or at least 6 hours after supplements containing polyvalent cations, including but not limited to the following products: cation-containing laxatives; Fe, Ca, or Mg supplements; and sucralfate. Monitor for virologic efficacy. DTG and supplements containing Ca or Fe can be taken simultaneously with food. Many oral multivitamins also contain varying amounts of polyvalent cations; the extent and significance of chelation is unknown.
Salmeterol	EVG/c EVG plus PI/r	↑ salmeterol possible	Do not coadminister due to potential increased risk of salmeterol-associated cardiovascular events.

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Key to Acronyms: Al = aluminum; ART = antiretroviral therapy; ARV = antiretroviral; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BID = twice daily; Ca = calcium; CaCO₃ = calcium carbonate; CCB = calcium channel blocker; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; c or COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; DTG = dolutegravir; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; Fe = iron; GI = gastrointestinal; INR = international normalized ratio; INSTI = integrase strand transfer inhibitor; Mg = magnesium; PAH = pulmonary arterial hypertension; PI = protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; PPI = proton pump inhibitor; RAL = raltegravir; SQV/r = saquinavir/ritonavir; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; Zn = zinc