

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

Updated: March 23, 2023

Reviewed: March 23, 2023

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 judgement 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 herbs 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
<b>Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia</b>		
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	No dose adjustment needed. Monitor blood pressure.
Terazosin	↔ terazosin expected	No dose adjustment needed.
Silodosin	↑ silodosin possible	No dose adjustment needed.
<b>Antibacterials—Antimycobacterials</b>		
Bedaquiline	↑ bedaquiline possible	Consider alternatives unless benefits outweigh risks. Monitor liver function and ECG for QTc prolongation.
Rifabutin	↓ LEN expected	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
Rifampin	LEN AUC ↓84%	Contraindicated.
Rifapentine	↓ LEN expected	Do not coadminister.
<b>Antibacterials—Macrolides</b>		
Azithromycin	↔ LEN expected	No dose adjustment needed.
Clarithromycin	↑ LEN possible	No dose adjustment needed.
Erythromycin	↑ LEN possible	No dose adjustment needed.
<b>Anticoagulants</b>		
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.
<b>Anticonvulsants</b>		
Carbamazepine	↓ LEN expected	Contraindicated.
Eslicarbazepine	↓ LEN expected	Do not coadminister. Consider alternative anticonvulsant or ARV.
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. Consider alternative anticonvulsant or ARV.
Phenobarbital	↓ LEN expected	Do not coadminister. Consider alternative anticonvulsant or ARV.
Phenytoin	↓ LEN expected	Contraindicated.

**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
Valproic Acid	↔ expected	No dose adjustment needed.
<b>Antidepressants, Anxiolytics, and Antipsychotics</b> 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.
Nefazodone	↑ LEN possible	No dose adjustment needed.
Trazodone	↑ trazodone expected	Administer lowest dose of trazodone and monitor for CNS and CV adverse events.
Tricyclic Antidepressants Amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, maprotiline, nortriptyline, protriptyline, trimipramine	↔ expected	No dose adjustment needed.
Selective Serotonin Reuptake Inhibitor Paroxetine	↑ paroxetine possible	Dose reduction may be necessary. Monitor for paroxetine-related adverse events.
Selective Serotonin Reuptake Inhibitors (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, sertraline)	↔ expected	No dose adjustment needed.
<b>Antipsychotics</b>		
Aripiprazole	↑ aripiprazole possible	No dose adjustment needed.
Brexipiprazole	↑ aripiprazole expected	If patient is known CYP2D6 poor metabolizer, then administer 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.
Lumateperone	↑ lumateperone expected	Recommended dose of lumateperone is 21 mg once daily.

**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
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	↔ expected	No dose adjustment needed.
Pimavanserin	↑ pimavanserin possible	No dose adjustment needed. Monitor ECG for QTc prolongation.
Pimozide	↑ pimozide expected	Do not coadminister.
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.
<b>Antifungals</b>		
Fluconazole	↔ expected	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.
<b>Antimalarials</b>		
Artemether/Lumefantrine	↑ artemether and lumefantrine possible	Monitor for lumefantrine-related adverse events, including QTc prolongation.
Atovaquone/Proguanil	↔ expected	No dose adjustment needed.
Mefloquine	↑ mefloquine possible	Monitor for mefloquine-related adverse events, including QTc prolongation.
<b>Antiplatelets</b>		
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.
<b>Antiretroviral Drugs</b>		
<i>CCR5 Antagonist</i>		
MVC	↔ expected	No dose adjustment needed.
<i>CD4 Post Attachment Inhibitor</i>		
IBA	↔ expected	No dose adjustment needed.
<i>gp120 Attachment Inhibitor</i>		
FTR	↔ expected	No dose adjustment needed.
<i>INSTIs</i>		
BIC, CAB (IM or PO), DTG, EVG/c, RAL	↔ expected	No dose adjustment needed.
<i>NRTIs</i>		
ABC, 3TC, FTC	↔ expected	No dose adjustment needed.
TAF	TAF AUC ↑ 32%	No dose adjustment needed.
TDF	TDF AUC ↑ 47%	No dose adjustment needed.
<i>NNRTIs</i>		
EFV	LEN AUC ↓ 56%	Do not coadminister.
ETR	↓ LEN expected	Do not coadminister.
DOR	↑ DOR possible	No dose adjustment needed.
NVP	↓ LEN expected	Do not coadminister.
RPV (IM or PO)	↑ RPV possible	No dose adjustment needed.
<i>PIs</i>		
ATV unboosted, 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.
LPV/r	↑ LEN expected	No dose adjustment needed.
<b>Antivirals—Orthopoxviruses (Mpox, Smallpox)</b>		
Brincidofovir	↔ 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
Cidofovir	↔ expected	No dose adjustment needed.
Tecovirimat	↓ LEN possible	No dose adjustment needed.
<b>Beta-Agonists, Long-Acting Inhaled</b>		
Arformoterol, Formoterol, Indacaterol, Olodaterol, Salmeterol	↔ expected	No dose adjustment needed.
<b>Cardiac Medications</b>		
Amiodarone	↑ amiodarone expected ↑ LEN possible	Do not coadminister.
Disopyramide	↑ disopyramide expected	Do not coadminister.
Lidocaine, Propafenone	↑ lidocaine possible ↑ propafenone possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor for antiarrhythmic-related adverse events and monitor concentrations, if available.
Dofetilide, Fecainide, Mexiletine	↔ expected	No dose adjustment needed.
Dronedarone	↑ dronedarone possible ↑ LEN possible	Consider alternative ARV or cardiac medication. If coadministered, monitor for dronedarone-related adverse events.
Quinidine	↑ quinidine expected	Do not coadminister.
Beta Blockers (e.g., carvediol, metoprolol, timolol)	↔ expected	No dose adjustment needed.
Bosentan	↓ LEN expected	Do not coadminister.
<b>Calcium Channel Blockers</b>		
Diltiazem, Verapamil	↑ diltiazem and verapamil possible	Monitor and dose adjust according to clinical response and adverse events.
Digoxin	↑ digoxin expected	Consider alternative ARV or antiarrhythmic. If coadministered, monitor digoxin therapeutic concentration.
Eplerenone	↑ eplerenone expected	For Post-MI CHF <ul style="list-style-type: none"> <li>• Dosing of eplerenone should not exceed 25 mg daily.</li> </ul> For Hypertension <ul style="list-style-type: none"> <li>• Initiate at 25 mg once daily. Dosing may be increased to a maximum of 25 mg twice daily.</li> </ul>

**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
Ranolazine	↑ ranolazine expected	Limit ranolazine to 500 mg twice daily.
Ivabradine	↑ ivabradine expected	Do not coadminister.
<b>Corticosteroids</b>		
Beclomethasone Inhaled or intranasal Ciclesonide Inhaled	↔ expected	No dose adjustment needed.
Budesonide, Fluticasone, Mometasone Inhaled or intranasal	↑ budesonide, fluticasone, mometasone 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	↔ expected	No dose adjustment needed.
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.
<b>Glucose-Lowering Medications</b>		
Canagliflozin	↔ expected	No dose adjustment needed.
Saxagliptin	↑ saxagliptin possible	No dose adjustment needed.
Dapagliflozin/Saxagliptin	↑ saxagliptin possible	No dose adjustment needed.
<b>Hepatitis C Direct-Acting Antiviral Agents</b>		
Elbasvir/Grazoprevir	↔ expected	No dose adjustment needed.
Glecaprevir/Pibrentasvir	↔ expected	No dose adjustment needed.
Ledipasvir/Sofosbuvir	↔ 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
Sofosbuvir/Velpatasvir	↔ expected	No dose adjustment needed.
Sofosbuvir/Velpatasvir/Voxilaprevir	↔ expected	No dose adjustment needed.
<b>Herbal Products</b>		
St. John's Wort	↓ LEN expected	Contraindicated.
<b>Hormonal Therapies</b>		
Contraceptives—Injectable Depot MPA	↑ MPA possible	No dose adjustment needed.
Contraceptives—Oral Drosperinone, Ethinyl Estradiol, Levonorgestrel, Norethindrone, Norgestimate  Subdermal Implant Etonogstrel  Subdermal Implant Levonorgestrel  Transdermal Ethinyl Estradiol/Norelgestromin  Vaginal Ring Etonogestrel/Ethinyl Estradiol  Vaginal Ring Segesterone/Ethinyl Estradiol	↑ contraceptive exposures possible	No dose adjustment needed.
Emergency Contraceptives Levonorgestrel (oral)	↑ levonorgestrel possible	No dose adjustment needed.
<b>Gender-Affirming Therapy</b>		
Estradiol, Goserelin, Leuprolide Acetate, Finasteride	↔ expected	No dose adjustment needed.
Dutasteride, Testosterone	↑ dutasteride and testosterone possible	No dose adjustment needed.
<b>Menopausal Hormone Replacement Therapy</b>		
Conjugated Estrogen (equine and synthetic), Micronized Progesterone, Medroxyprogesterone	↑ estrogen and progesterone possible	No dose adjustment needed.
Drospirenone	↑ drospirenone possible	No dose adjustment needed.
<b>Immunosuppressants</b>		



**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
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.
<b>Lipid-Modifying Agents</b>		
Atorvastatin	↑ atorvastatin possible	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.
<b>Narcotics and Treatment for Opioid Dependence</b>		
Buprenorphine Sublingual, buccal, or implant	↑ buprenorphine possible	<p><b>Initiation of Buprenorphine in Patients Taking LEN</b></p> <ul style="list-style-type: none"> <li>• Titrate buprenorphine dose to desired effect and use the lowest feasible initial dose.</li> </ul> <p><b>Initiation of LEN in Patients Taking Buprenorphine</b></p> <ul style="list-style-type: none"> <li>• Dose adjustment for buprenorphine may be needed. Monitor for buprenorphine-related adverse events.</li> </ul>
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	No dose adjustment needed.
Oxycodone	↑ oxycodone possible	Monitor for opioid-related adverse events, including potentially fatal

**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
		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.
<b>PDE5 Inhibitors</b>		
Avanafil	↑ avanafil expected	Avanafil dose should not exceed 50 mg once every 24 hours.
Sildenafil	↑ sildenafil expected	<p><b>For Treatment of Erectile Dysfunction</b></p> <ul style="list-style-type: none"> <li>Start with sildenafil 25 mg and monitor for sildenafil-related adverse events.</li> </ul> <p><b>For Treatment of PAH</b></p> <ul style="list-style-type: none"> <li>Reduce the dose of sildenafil to 20 mg three times a day when discontinuing treatment with LEN.</li> </ul>
Tadalafil	↑ tadalafil expected	No dose adjustment needed.
Vardenafil	↑ vardenafil expected	Vardenafil dose should not exceed 5 mg once every 24 hours.
<b>Sedative/Hypnotics</b>		
Alprazolam	↑ alprazolam expected	Consider lowest dose and monitor for alprazolam-related adverse events.
Clonazepam	↑ clonazepam possible	Consider alternative benzodiazepines.
Diazepam	↑ diazepam possible	Consider lowest dose and monitor for benzodiazepine-related events.
Lorazepam, Oxazepam, Temazepam	↔ expected	No dose adjustment needed.
Midazolam (Oral)	↑ midazolam expected	Use with caution and consider alternative benzodiazepine.
Suvorexant	↑ midazolam expected	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.
Triazolam	↑ triazolam expected	Use with caution and consider alternative benzodiazepine.
Zolpidem	↑ zolpidem possible	Consider initiating zolpidem at a low 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
<b>Miscellaneous Drugs</b>		
Cisapride	↑ cisapride expected	Do not coadminister.
Colchicine	↑ colchicine expected	For Treatment of Gout Flares <ul style="list-style-type: none"> <li>Administer single colchicine dose of 1.2 mg. Do not repeat dose for at least 3 days.</li> </ul> For Treatment of Familial Mediterranean Fever <ul style="list-style-type: none"> <li>Colchicine dose should not exceed 1.2 mg daily (may be given as 0.6 mg twice a day).</li> </ul>
Ergot Derivatives Dihydroergotamine, ergotamine, methylergonovine	↑ dihydroergotamine, ergotamine, methylergonovine expected	Do not coadminister.
Flibanserin	↑ flibanserin expected	Do not coadminister.
Naloxegol	↑ naloxegol expected	Avoid use; if coadministration is necessary, decrease dosage of naloxegol and monitor for naloxegol-related adverse events.

**Key to Symbols**

↑ = increase  
 ↓ = decrease  
 ↔ = no change

Key: 3TC = lamivudine; ABC = abacavir; AUC = area under the curve; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CAB = cabotegravir; CHF = congestive heart failure; CNS = central nervous system; CV = cardiovascular; CYP = cytochrome P 450; 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; LPV/r = lopinavir/ritonavir; MI = myocardial infarction; MPA = medroxyprogesterone acetate; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PAH = pulmonary arterial hypertension; PDE5 = phosphodiesterase type 5; PI = protease inhibitor; PO = orally; RAL = raltegravir; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate