

Table 19B: Lenacapavir (LEN) Interactions When Used for HIV Prevention [a,b] (also see prescribing information)		
Class or Drug	Mechanism of Action	Clinical Comments
Direct oral anticoagulants (DOACs; apixaban, rivaroxaban, dabigatran, edoxaban, etc.)	DOAC levels potentially increase due to effect on CYP3A4 and P-gP.	<ul style="list-style-type: none"> No dose adjustment needed; monitor for increased risk of bleeding. Refer to DOAC prescribing information for use with moderate CYP3A4 and P-gP inhibitors.
Digoxin	Moderate inhibition of P-gP potentially increases digoxin levels.	Monitor digoxin concentrations when using with LEN.
Anticonvulsants	Carbamazepine, eslicarbazepine, oxcarbazepine, phenobarbital, phenytoin, primidone: CYP3A4 and P-gP induction potentially decreases LEN levels.	<p>Carbamazepine, oxcarbazepine, phenytoin (strong CYP3A4 inducers):</p> <ul style="list-style-type: none"> Consider alternative anticonvulsants such as levetiracetam. At initiation of strong CYP3A4 inducer in patients already using LEN PrEP, see Table 4 of the Yeztugo prescribing information (page 6) for instructions on administering a supplemental dose of LEN PrEP. After stopping use of strong CYP3A4 inducer, continue to administer LEN PrEP every 6 months as scheduled without supplemental subcutaneous or oral dosing. Supplemental dosing only continues until the patient has stopped the inducer. <p>Eslicarbazepine, phenobarbital, primidone (moderate CYP3A4 inducers):</p> <ul style="list-style-type: none"> Consider alternative anticonvulsants such as levetiracetam. At initiation of moderate CYP3A4 inducer in patients already using LEN PrEP, see Table 5 of the Yeztugo prescribing information (page 6) for instructions on administering a supplemental dose of LEN PrEP. After stopping use of moderate CYP3A4 inducer, continue to administer LEN PrEP every 6 months as scheduled without supplemental subcutaneous dosing. Supplemental dosing only continues until the patient has stopped the inducer.
Antipsychotics	Pimozide: Moderate inhibition of P-gP potentially increases pimozide levels.	Pimozide: Do not coadminister.
Cardiac medications	Amiodarone, disopyramide, quinidine, ivabradine: Moderate inhibition of P-gP potentially increases cardiac medication levels.	Amiodarone, disopyramide, quinidine, ivabradine: Do not coadminister.
Rifabutin, rifampin, rifapentine	CYP3A4 and P-gP induction associated with rifamycins potentially decreases LEN levels.	<ul style="list-style-type: none"> At initiation of strong CYP3A4 inducer in patients already using LEN PrEP, see Table 4 of the Yeztugo prescribing information (page 6) for instructions on administering a supplemental dose of LEN PrEP.

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		<ul style="list-style-type: none"> After stopping use of strong CYP3A4 inducer, continue to administer LEN PrEP every 6 months as scheduled without supplemental subcutaneous or oral dosing. Supplemental dosing only continues until the patient has stopped the inducer.
Dexamethasone, hydrocortisone (systemic)	<ul style="list-style-type: none"> Moderate inhibition of CYP3A4 and P-gP potentially increases corticosteroid concentrations and the related risk of Cushing's syndrome and adrenal suppression. Dexamethasone (systemic): Decreased LEN levels expected with dexamethasone doses >16 mg/day. 	<p>Dexamethasone (doses >16 mg/day):</p> <ul style="list-style-type: none"> At initiation of moderate CYP3A4 inducer in patients already using LEN PrEP, see Table 5 of the Yeztugo prescribing information (page 6) for instructions on administering a supplemental dose of LEN PrEP. After stopping use of moderate CYP3A4 inducer, continue to administer LEN PrEP every 6 months as scheduled without supplemental subcutaneous dosing. Supplemental dosing only continues until the patient has stopped the inducer.
Ergotamine derivatives (dihydroergotamine, ergotamine, methylergonovine, etc.)	Moderate inhibition of CYP3A4 potentially increases ergotamine derivative levels.	Do not coadminister.
St. John's wort	CYP3A4 and P-gP induction potentially decreases LEN levels.	Do not coadminister. Consider other alternatives to LEN for HIV prevention.
Lovastatin, simvastatin, lomitapide	Lovastatin, simvastatin, lomitapide: Moderate inhibition of CYP3A4 and P-gP potentially increases levels.	<ul style="list-style-type: none"> Simvastatin, lovastatin: Initiate at lowest dose and titrate to achieve clinical effect; monitor closely for statin toxicity. Lomitapide: Concomitant use is contraindicated.
Opioids metabolized via CYP3A (i.e., fentanyl, oxycodone, tramadol)	Moderate inhibition of CYP3A4 potentially increases opioid levels.	<ul style="list-style-type: none"> Monitor for therapeutic effects and adverse reactions associated with CYP3A-metabolized opioid analgesics, including potentially fatal respiratory depression. Tramadol: Consider tramadol dose reduction with concomitant use.
Methadone, buprenorphine	Moderate inhibition of CYP3A4 and P-gP potentially increases methadone or buprenorphine levels.	<ul style="list-style-type: none"> Patients initiating MAT while already on LEN: Initiate MAT at lowest initial or maintenance dose. Patients initiating LEN while already on MAT: MAT dose adjustments may be needed. Monitor for excess sedation and/or respiratory depression.
Naloxegol (opioid antagonist)	Moderate inhibition of CYP3A4 potentially increases naloxegol levels.	Avoid concomitant use. If use is required, decrease naloxegol dose and monitor for adverse effects.

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PDE5 inhibitors	Moderate inhibition of CYP3A4 and P-gp potentially increases PDE5 inhibitor levels.	<p>For pulmonary hypertension:</p> <ul style="list-style-type: none"> • Tadalafil: Concomitant use is not recommended. • For other medications, refer to dosing guidelines. <p>For erectile dysfunction, refer to prescribing information and guidance listed below:</p> <ul style="list-style-type: none"> • Avanafil: Do not coadminister. • Sildenafil: Start with 25 mg every 48 hours; monitor for adverse effects. • Tadalafil: Start with 5 mg and do not exceed 10 mg every 72 hours; monitor for adverse effects. <p>Vardenafil: Administer 2.5 mg every 72 hours; monitor for adverse effects.</p>
Midazolam (oral), triazolam	Moderate inhibition of CYP3A4 and P-gp potentially increases sedative levels.	Use with caution; monitor for excess sedation.
ADHD medications	Modafinil: CYP3A4 induction may reduce LEN levels.	Modafinil: Consider alternative ADHD medications.
<p>Abbreviations: ADHD, attention-deficit/hyperactivity disorder; ARV, antiretroviral; COBI, cobicistat; CYP, cytochrome P450; MAT, medication-assisted therapy; PDE5, phosphodiesterase type 5; P-gp, P-glycoprotein; PI, protease inhibitor; PrEP, pre-exposure prophylaxis; RTV, ritonavir; TDM, therapeutic drug monitoring.</p> <p>Notes:</p> <p>a. For LEN as HIV PrEP, see prescribing information for Yeztugo; for LEN as HIV treatment, see Table 19A: Lenacapavir Interactions When Used for HIV Treatment and prescribing information for Sunlenca.</p> <p>b. For individuals using subcutaneous LEN every 6 months for HIV prevention. No guidance is currently available for (1) individuals using weekly oral LEN for HIV prevention or (2) initiating subcutaneous LEN in individuals already using strong or moderate CYP3A4 inducers.</p> <p>No significant interactions/no dose adjustments necessary (see guideline section Drug-Drug Interactions by Common Medication Class): Common oral antibiotics; antihypertensive medications; antiplatelet medications; antidiabetic medications; acid-reducing agents; polyvalent cations; asthma and allergy medications; long-acting beta agonists; antidepressants; sleep medications; antipsychotics; nonopioid pain medications; hormonal contraceptives; alpha-adrenergic antagonists for benign prostatic hyperplasia; tobacco and smoking cessation products; alcohol, disulfiram, and acamprosate; immunosuppressants; COVID-19 therapeutics; mpox treatments; gender-affirming hormones.</p>		