Interactions with Lenacapavir as Antiretroviral Therapy

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Summary of drug-drug interactions with lenacapavir

Lenacapavir is an HIV-1 capsid inhibitor, licensed as a therapeutic addition to antiretroviral regimens in individuals with multidrug-resistant HIV-1, and is administered subcutaneously every 6 months following an oral loading dose.

- Lenacapavir undergoes minimal metabolism; drugs impacting lenacapavir and preventing its use are essentially moderate and strong inducers of drug metabolizing enzymes.
- Lenacapavir is a moderate inhibitor of CYP3A4 and therefore impacts essentially sensitive and/or narrow therapeutic index CYP3A4 substrates.
- Upon discontinuation of lenacapavir, residual concentrations of lenacapavir may remain in the circulation for prolonged periods and could affect the exposure of sensitive and/or narrow therapeutic index CYP3A4 substrates initiated within 9 months after the last subcutaneous dose.

Comedications contraindicated or not recommended with lenacapavir

This list of medicines is not exhaustive and is subject to change.

Therapeutic class	Comedication	Potential consequence of the interaction
Antiarrhythmics	Amiodarone, Disopyramide, Quinidine	Risk of cardiac arrhythmias.
Antibacterials	Rifabutin, Rifampicin, Rifapentine	Potential loss of lenacapavir efficacy.
Antiplatelets	Clopidogrel	Decreased conversion to the active metabolite of clopidogrel leading potential to loss of efficacy.
Anticonvulsants	Carbamazepine, Cenobamate, Eslicarbazepine, Oxcarbazepine, Phenobarbital, Phenytoin, Primidone	Potential loss of lenacapavir efficacy.
Antifungals	Griseofulvin	Potential loss of lenacapavir efficacy.
Antihistamines	Astemizole, Terfenadine,	Risk of cardiac arrhythmias.
Antimigraine agents	Dihydroergotamine, Ergotamine	Risk of vasospasm leading to cerebral ischemia and/or ischemia of the extremities.
Antiprotozoals	Halofantrine	Risk of cardiac arrhythmias.
Antipsychotics	Cariprazine	Accumulation of cariprazine and its metabolite.
	Pimozide	Risk of QT prolongation and Torsades de Pointes ventricular tachycardia.
	Thioridazine	Potential loss of lenacapavir efficacy.
Antiretrovirals	Atazanavir, Atazanavir/cobicistat, Atazanavir/ritonavir	Significant increase in lenacapavir exposure which can increase the risk of adverse effects.
	Efavirenz, Etravirine, Nevirapine	Potential loss of lenacapavir efficacy.
Cancer therapies	Apalutamide, Bexarotene, Dabrafenib, Enasidenib, Enzalutamide, Ifosfamide, Ivosidenib, Lorlatinib, Mitotane, Sotorasib, Vemurafenib	Potential loss of lenacapavir efficacy.
	Avapritinib, Bosutinib, Entrectinib, Infigratinib, Neratinib, Pemigatinib, Pexidartinib, Regorafenib	Significant increase in the cancer drug exposure which can result in adverse events.
Gastrointestinal agents	Cisapride, Domperidone	Risk of cardiac adverse events.
Herbals	Guggulsterone, St John's Wort	Potential loss of lenacapavir efficacy.
Hypertension / Heart failure agents	Bosentan	Potential loss of lenacapavir efficacy.
	Tadalafil	Significant increase in tadalafil exposure which can result in adverse events.
Illicit / Recreational	Nitazenes	Increase in nitazene exposure which can result in serious adverse events.
Lipid lowering agents	Lomitapide	Significant increase in lomitapide exposure which can result in adverse events.
Others	Modafinil, Ursodeoxycholic acid	Potential loss of lenacapavir efficacy.
	Ergometrine, Methylergometrine	Risk of acute ergot toxicity.
	Flibanserin	Risk of severe hypotension and syncope.
Steroids	Betamethasone, Dexamethasone (dose >16 mg)	Potential loss of lenacapavir efficacy.

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Comedications which can be coadministered with lenacapavir but which may be impacted by lenacapavir residual CYP3A4 inhibition upon treatment discontinuation

This list of medicines is not exhaustive and is subject to change.

Therapeutic Class	Comedications
Anaesthetics and Muscle Relaxants	Ketamine
Analgesics	Alfentanil, Dextropropoxyphene, Fentanyl
Anti-coagulants	Phenprocoumon, Warfarin
Anticonvulsants	Ethosuximide
Antiprotozoals	Quinine
Antipsychotics/Neuroleptics	Lurasidone, Quetiapine
Anxiolytics/Hypnotics/ Sedatives	Alprazolam, Buspirone, Chlordiazepoxide, Clorazepate, Estazolam, Flurazepam, Midazolam, Triazolam
Calcium Channel Blockers	Felodipine, Nifedipine, Nisoldipine, Nitrendipine
Cancer Therapies	Abemaciclib, Acalabrutinib, Bortezomib, Busulfan, Cobimetinib, Copanlisib, Cyclophosphamide, Dasatinib, Docetaxel, Encorafenib, Erlotinib, Everolimus, Ibrutinib, Irinotecan, Lapatinib, Paclitaxel, Romidepsin, Temsirolimus, Thiotepa, Toremifene, Trastuzumab emtansine, Venetoclax, Vinblastine, Vincristine, Vinorelbine
Erectile Dysfunctional Agents	Avanafil, Sildenafil, Tadalafil, Vardenafil
Herbals/Supplements	Red yeast rice
Hypertension / Heart Failure Agents	Doxazosin, Eplerenone, Finerenone, Ivabradine, Lacidipine, Lercanidipine, Macitentan, Ranolazine, Sildenafil
Immunosuppressants	Ciclosporin, Everolimus, Sirolimus, Tacrolimus
Lipid Lowering Agents	Lovastatin, Simvastatin
Other	Alfuzosin, Bromocriptine, Colchicine, Dapoxetine

Drug interactions with lenacapavir and other antiretroviral agents

Interaction	ARV Class	ARV Drugs
No pharmacokinetic interaction expected	Integrase Inhibitors	Cabotegravir, Dolutegravir, Raltegravir
	NNRTIs	Dapivirine
	NRTIs	Abacavir, Emtricitabine, Islatravir, Lamivudine, Zidovudine
	Other	Albuvirtide, Enfuvirtide, Fostemsavir, Ibalizumab
No dose adjustment needed: any increase in exposure is unlikely to be clinically relevant	Integrase Inhibitors	Bictegravir (potential ↑ bictegravir exposure)
		Elvitegravir/cobicistat (lenacapavir AUC ↑ 128%)
	NNRTIs	Doravirine (potential ↑ doravirine exposure)
		Rilpivirine (potential ↑ rilpivirine exposure)
	NRTIs	Tenofovir alafenamide (TAF AUC ↑ 32%; TFV AUC ↑ 47%)
		Tenofovir-DF (potential ↑ TDF or ↑ TFV)
	PIs	Darunavir/ ritonavir (potential ↑ lenacapavir exposure)
		Darunavir/ cobicistat (lenacapavir AUC ↑ 94%)
		Lopinavir/ ritonavir (potential ↑ lenacapavir exposure)
	Other	Maraviroc (potential ↑ maraviroc exposure; no a priori dose adjustment needed in the absence of boosted antiretroviral agents)
Coadministration not recommended: potential significant decrease in lenacapavir exposure	NNRTIs	Efavirenz (lenacapavir AUC ↓ 56%)
		Etravirine (potential significant ↓ lenacapavir exposure)
		Nevirapine (potential significant ↓ lenacapavir exposure)
Coadministration not recommended: potential significant increase in lenacapavir exposure	PIs	Atazanavir alone (potential significant ↑ lenacapavir exposure)
		Atazanavir/ ritonavir (potential significant ↑ lenacapavir exposure)
		Atazanavir/cobicistat (lenacapavir AUC ↑ 321%)

Lenacapavir Product Labels

Sunlenca Summary of Product Characteristics, Gilead Sciences Ltd.

Sunlenca Prescribing Information, Gilead Sciences Inc.

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