GILEAD | Medical Information

Yeztugo® (lenacapavir) Coadministration with Fluconazole

This document is in response to your request for information regarding Yeztugo® (lenacapavir [LEN]) and coadministration with fluconazole.

Some data may be outside of the US FDA-approved Prescribing Information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA approved prescribing information.

The full indication, important safety information, and boxed warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_pi.

PK DDI Evaluation

The interaction has not been studied between LEN and fluconazole. Based on the PK profile of LEN and fluconazole, a PK interaction would not be predicted.[1] For more information about fluconazole, please refer to its product labeling.[2]

LEN PK[1,3]

DDI Mechanism		LEN
Drug Transporters	OCT2	NA
	MATE1	NA
	P-gp	Substrate[a], and Weak Inhibitor
	BCRP	Weak Inhibitor
	OATP1B1	NA
	OATP1B3	NA
Drug Metabolizing Enzymes	CYP3A	Substrate[a,b], and Moderate inhibitor
	UGT1A1	Substrate[a]

[a]Combined P-gp, UGT1A1, and strong CYP3A inhibitors may significantly increase plasma concentrations of LEN. Concomitant administration of LEN with these inhibitors is not recommended.
[b]Drugs that are strong or moderate inducers of CYP3A may significantly decrease plasma concentrations of LEN, which may result in reduced effectiveness of LEN. Therefore, dosage modifications (supplemental doses) of LEN are recommended when initiating strong or moderate CYP3A inducers. Please refer to Section 2.5, *Dosage Modifications for Co-administration with Strong or Moderate CYP3A Inducers*, of the Yeztugo US Prescribing Information for more information.

Dosing Recommendations for Individuals Receiving LEN and Initiating Therapy with Strong CYP3A[a] Inducers[1]

Maintain Scheduled Continuation Injection Dosing	Schedule for Supplemental Doses of LEN	
	Time	**Dosage**
Continue to administer once every 6-months scheduled continuation dosing of LEN 927 mg subcutaneously (2 x 1.5 mL injections), plus administer supplemental doses of LEN as shown in this table	On day strong CYP3A inducer is initiated (which should be at least 2 days after LEN is first initiated)	**Supplemental dosage: Step 1** 927 mg subcutaneously (2 x 1.5 mL injections) and 600 mg orally (2 x 300 mg tablets)
	On day after strong CYP3A inducer is initiated	**Supplemental dosage: Step 2** 600 mg orally (2 x 300 mg tablets)
	If strong CYP3A inducer is co-administered for longer than 6 months	**Subsequent supplemental dosage:** Every 6-months[b] from initiation of strong CYP3A inducer, continue to administer supplemental doses of LEN as described above in Steps 1 and 2.
	After stopping the strong CYP3A inducer, continue the once every 6-months scheduled continuation injection dosing of LEN	

[a]Dosing recommendations are not available for the initiation of LEN in individuals already receiving strong CYP3A inducers, nor in individuals receiving the weekly oral dosage of LEN.
[b]26 weeks +/-2 weeks.

Dosing Recommendations for Individuals Receiving LEN and Initiating Therapy with Moderate CYP3A[a] Inducers[1]

Maintain Scheduled Continuation Injection Dosing	Schedule for Supplemental Doses of LEN	
	Time	**Dosage**
Continue to administer once every 6-months scheduled continuation dosing of LEN 927 mg subcutaneously (2 x 1.5 mL injections), plus administer supplemental doses of LEN as shown in this table	On day moderate CYP3A inducer is initiated	**Supplemental dosage** 463.5 mg subcutaneously (1 x 1.5 mL injections)
	If moderate CYP3A inducer is co-administered for longer than 6 months	**Subsequent supplemental dosage** Every 6-months[b] from initiation of moderate CYP3A inducer, continue to administer a supplemental dose of LEN as described above.
	After stopping the moderate CYP3A inducer, continue the once every 6-months scheduled continuation injection dosing of LEN	

[a]Dosing recommendations are not available for the initiation of LEN in individuals already receiving moderate CYP3A inducers, nor in individuals receiving the weekly oral dosage of LEN.
[b]26 weeks +/-2 weeks.

Relevant LEN Label Information[1]

There is no information in the LEN product labeling about the coadministration of LEN and fluconazole.

Available Data

There are no Gilead studies evaluating the coadministration of LEN and fluconazole.

Additionally, a literature search was conducted in Ovid MEDLINE and Embase databases for studies published between 1946 and June 30, 2025 using search terms that included Yeztugo, lenacapavir, fluconazole, and related search terms. No relevant citations were found.

References

1. Enclosed, Gilead Sciences Inc. YEZTUGO® (lenacapavir) tablets, for oral use. YEZTUGO® (lenacapavir) injection, for subcutaneous use. U.S. Prescribing Information. Foster City, CA.
2. Pfizer, Inc. DIFUCAN® (fluconazole tablets, fluconazole powder, for suspension). U.S. Prescribing Information. New York, NY.
3. Lutz J. CLINICAL EVALUATION OF DRUG INTERACTIONS WITH ORAL LENACAPAVIR AND PROBE DRUGS [Presentation]. Paper presented at: Conference on Retroviruses and Opportunistic Infections (CROI); March 6-10, 2021; Virtual.

Abbreviations

BCRP=breast cancer resistance protein
DDI=drug-drug interaction
LEN=lenacapavir
MATE=multidrug and toxin extrusion protein
NA=not applicable
OATP=organic anion transporting polypeptide
OCT=organic cation transporter
P-gp=P-glycoprotein
PK=pharmacokinetic(s)
UGT=uridine 5'-diphospho-glucuronosyltransferase

Product Label

For the full indication, important safety information, and boxed warning, please refer to the Yeztugo US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_pi.

Follow-Up

For any additional questions, please contact Gilead Medical Information at:

☎1-866-MEDI-GSI (1-866-633-4474) or 🖱 www.askgileadmedical.com

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Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or
🖱 www.gilead.com/utility/contact/report-an-adverse-event

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

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