clinical cases DDIs

Date of report 08 Oct 2026

Reported case interaction between **Lenacapavir LA** and **Rifabutin**

Drugs suspected to be involved in the DDI

Victim
Lenacapavir LA

Daily Dose
1390 (mg)

Dose adjustment performed
Yes

Administration Route
Subcutaneous

Start date
Aug. 15, 2025

End date
Ongoing

Perpetrator
Rifabutin

Daily Dose
150 (mg)

Dose adjustment performed
Yes

Administration Route
Oral

Start date
July 15, 2025

End date
Ongoing

Complete list of drugs taken by the patient

Antiretroviral treatment

Lenacapavir LA
Darunavir (with Ritonavir or Cobicistat)

Complete list of all comedications taken by the patient, included that involved in the DDI

No other drugs

Clinical case description

Gender

Male

Age

30

eGFR (mL/min)

>60

Liver function impairment

No

Description

In June 2025, a 30-year-old male with multidrug resistant HIV and a history of non-adherence (pre-admission CD4 count <10 cells/mm3, HIV RNA 28'000 copies/mL) was hospitalized for respiratory failure secondary to Pneumocystis jirovecii pneumonia along with disseminated Mycobacterium avium complex (MAC) infection. Treatment for HIV included dolutegravir, lamivudine, darunavir/ritonavir and tenofovir DF during hospitalization. In late July 2025, rifabutin was added to the MAC treatment regimen to enhance efficacy. A reduced dose of 150 mg daily was selected because of concomitant darunavir/ritonavir use. Following achievement of virological suppression (HIV RNA <20 copies/mL), ART was simplified to lenacapavir plus daily darunavir/ritonavir to address ongoing adherence challenges.

Of note, fostemsavir was considered suboptimal because of its twice-daily dosing schedule in a patient with adherence challenges, while ibalizumab was not an option because it was not routinely available in the country where this case occurred.

At the time of lenacapavir initiation, the patient had already been receiving rifabutin for one month; therefore, its maximal enzyme inducing effect was assumed to have been reached. To compensate for rifabutin-mediated induction, the oral lenacapavir loading dose was increased to 900 mg (instead of the 600 mg standard dose) on days 1 and 2. Similarly, the subcutaneous dose was increased to 1390 mg (instead of the standard 927 mg), administered on day 1 and every six month thereafter.

The decision to increase the lenacapavir dose was driven by the need to achieve adequate drug exposure without delay, considering that the maximal enzyme inducing effect of rifabutin had already been reached at the time of lenacapavir initiation. The original oral ART regimen was continued for the first following lenacapavir initiation. Therapeutic drug monitoring (TDM) of lenacapavir was performed daily during the first week, weekly for the first month, and subsequently at months 2 through 5. Lenacapavir concentrations consistently remained above the target threshold of 15.5 ng/mL. Specifically, lenacapavir concentrations were 3-fold above this threshold at week 1, 4-fold above it at weeks 2 and 3, and increased to 15-fold above the threshold at months 3 and 4, before declining to 1.2 fold above the threshold by month 6. Initial lenacapavir concentrations were comparable to those reported in real-world clinical practice (Le MP et al. CROI 2025), suggesting that the increased lenacapavir successfully compensated for rifabutin mediated induction. At months 3 and 4, lenacapavir concentrations exceeded twice the C_{max} reported in the lenacapavir prescribing, potentially reflecting

the effect of concomitant darunavir/ritonavir. Indeed, coadministration of lenacapavir with darunavir/cobicistat has been shown to increase lenacapavir AUC and Cmax by 94% and 130%, respectively. The patient viral load remained suppressed throughout lenacapavir therapy
This case demonstrates that dose adjusted lenacapavir can achieve therapeutic exposure despite the concurrent use of a moderate CYP3A4 inducer.
This case has been presented at the 27th International wokshop on HIV clinical pharmacology, Montreal, September 2-3, 2026.

Clinical Outcome

No unwanted outcome

Editorial Comment

This is an interesting and well-documented case, particularly given the availability of lenacapavir therapeutic drug monitoring (TDM) data. Its main educational value lies in the use of TDM to support individualized dosing in a complex interaction scenario involving both an inducer, rifabutin, and an inhibitor, ritonavir.
Coadministration of lenacapavir and rifabutin has not been studied and is not recommended. Lenacapavir is a substrate of CYP3A4, P-gp and UGT1A1. Coadministration with the moderate CYP3A4 inducer efavirenz reduced lenacapavir AUC and Cmax by 56% and 36%, respectively. A similar effect may occur with rifabutin, potentially leading to loss of therapeutic effect and development of resistance.

The patient was also receiving darunavir/ritonavir (DRV/r), which adds further pharmacokinetic complexity. Coadministration of lenacapavir with darunavir/cobicistat increased lenacapavir AUC and Cmax by approximately 94% and 130%, respectively, and a similar effect is expected with DRV/r. Although this interaction alone is not considered clinically significant and does not require lenacapavir dose adjustment, rifabutin introduces an opposing inducing effect.
Despite coadministration being discouraged in the prescribing information, the individualized lenacapavir dose adjustment, supported by close TDM, allowed concomitant treatment in this patient while maintaining concentrations above the proposed target and sustained virological suppression.
This case highlights the value of TDM in assessing drug exposure in the presence of concomitant induction and inhibition and supporting individualized management. However, it does not establish an optimal dosing strategy or determine whether standard lenacapavir dosing would have provided adequate exposure.

University of Liverpool Recommendation

- These drugs should not be coadministered

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Personal information from the specialist

Name
Catia

Surname
Marzolini

Institution
University Hospital of Basel
University of Liverpool

Country
CH

Other authors

Name
Catia

Surname
Marzolini

Institution
University Hospital Lausanne