Real-World Medication Use and Potential Interactions With Lenacapavir for HIV PrEP

Poster 1062

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Conclusions

- Most (83.8%) HIV pre-exposure prophylaxis (PrEP) users in the US were taking concomitant prescription medications in 2024
- Among PrEP users with concomitant medication use, 86.9% were taking medications that, if taken with lenacapavir, would not require monitoring for side effects or dose modifications of either medication
- Only 0.5% of PrEP users had concomitant use of a strong or moderate cytochrome P450 3A (CYP3A) inducer that would require a lenacapavir dose modification
- Fewer than 13% of PrEP users had concomitant use of a sensitive CYP3A and/or P-glycoprotein (P-gp) substrate in 2024 that would require monitoring for side effects or dose modification when taken with lenacapavir; the most common was erectile dysfunction medication (11%)
- These findings underscore the low prevalence of clinically significant potential lenacapavir drug-drug interactions (DDI) among real world PrEP users

Plain Language Summary

Lenacapavir is a new medication to prevent HIV ("PrEP") that became available in 2025.

Because lenacapavir can affect how some medications work when they are taken together, we looked at what medications people were using at the same time as PrEP in 2024, before lenacapavir became available.

We found that most of the medicines people used were expected to work safely with lenacapavir. Only a small number of people were taking medicines that might need a lower dose if used together with lenacapavir.

References: **1.**Yeztugo® Prescribing Information. Available at: https://www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_pi.pdf (accessed Feb 2026). **2**. Di Perri G. *Infez Med*. 2023;31:495–99. **3**. HIV Drug Interactions. Available at: https://hiv-druginteractions.org/checker (accessed Feb 2026). **4**. Yeytuo® Summary of Product Characteristics. Available at https://www.ema.europa.eu/en/documents/product-information/yeytuo-epar-product-information_en.pdf (accessed Feb 2026). **5**. IQVIA Real World & Health Datasets. Available at: https://www.iqvia.com/solutions/real-world-evidence/real-world-data-and-insights (accessed Feb 2026). **6**. Blumenthal J, et al. Poster P-305 presented at: IDWeek: October 19–22, 2025, Atlanta, GA.

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Background

- Individuals using PrEP for HIV-1 prevention may be using other medications concomitantly
- Lenacapavir is a twice-yearly injectable HIV-1 capsid inhibitor that was FDA-approved in 2025 for HIV-1 PrEP in the US[1]
- Lenacapavir-for-PrEP may have clinically significant DDIs with some medications[1–4]
  - As a substrate of CYP3A, P-gp, and UGT1A1, lenacapavir concentrations may be decreased by strong or moderate inducers of CYP3A
  - Lenacapavir is a moderate inhibitor of CYP3A and P-gp; co-administration of lenacapavir with sensitive substrates of CYP3A and/or P-gp may increase concentrations of these substrates

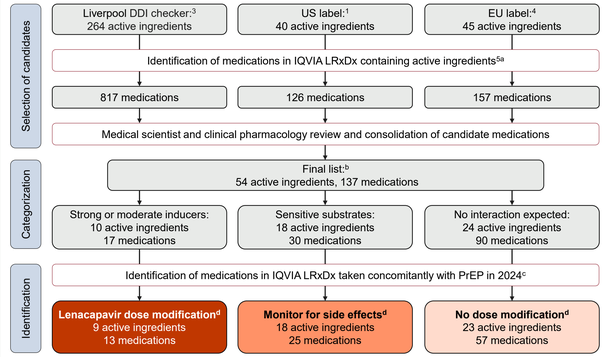
Objective

- To explore real-world use of medications metabolized through CYP3A and/or P-gp with potential lenacapavir DDIs among PrEP users not currently receiving lenacapavir in the US

Methods

- **Figure 1** shows a schematic of the process used to identify and categorize potential DDIs with lenacapavir-for-PrEP
- HIV-1 negative individuals in the US with ≥1 dispensed oral or injectable PrEP prescription between January 1 and December 31, 2024, were identified in the IQVIA LRxDx database[5]
- Concomitant medications were defined as dispensed prescriptions that chronologically overlapped a PrEP prescription
- Medications metabolized through CYP3A and/or P-gp with potential lenacapavir DDIs were identified using the HIV Drug Interactions Checker by the University of Liverpool and the US and EU product labels for lenacapavir-for-PrEP[1,3,4]
- Concomitant medications were categorized by recommended action for use with lenacapavir based on the US label as follows:
  1. Strong or moderate CYP3A inducers requiring lenacapavir dose modification
  2. Sensitive substrates of CYP3A and/or P-gp requiring monitoring for side effects/possible dose modification of the concomitant medication
  3. Metabolized through CYP3A and/or P-gp but no clinically significant interaction expected; no dose modification needed for either medication
- Individuals taking multiple concomitant medications were included under the highest category of DDI they received
- Overall frequency of use, and frequency and duration of concomitant use were assessed for medications in each lenacapavir DDI category

Figure 1. Identification of Concomitant Medications Metabolized Through CYP3A and/or P-gp and Categorization by Potential Lenacapavir DDIs



[a]Real-world claims were reviewed to confirm drug dosage, formulation, and route of administration aligned with Liverpool DDI checker guidelines and the US and EU label for suggested active ingredients. [b]Categories were assigned based on recommendations provided in the US label for concomitant use with lenacapavir, excluding topical routes of administration. Ingredients/medications were counted separately when used for different indications or dosages. [c]Concomitant medications were defined as prescriptions that chronologically overlapped with a PrEP prescription (Jan 1 – Dec 31, 2024). [d]Full list of active ingredients is included in **Table 2**.

DDI, drug-drug interaction; LRxDx, longitudinal prescription and diagnosis dataset; PrEP, pre-exposure prophylaxis.

Results

Population Characteristics

- In total, 457,402 PrEP users in 2024 were identified in the US
- Mean age of all PrEP users was 38 years; 90.9% were male, and 89.8% used commercial health insurance (**Table 1**)

Table 1. Cohort Characteristics

	All PrEP users	PrEP users with any concomitant medication	PrEP users with a concomitant medication metabolized through CYP3A and/or P-gp
Total, n (%)	457,402 (100)	383,221 (83.8)	118,531 (25.9)
Mean (SD) age, years	38.0 (12.3)	38.8 (12.5)	40.0 (12.9)
Sex at birth, n (%)			
Male	415,554 (90.9)	349,539 (91.2)	108,521 (91.6)
Female	41,837 (9.2)	33,675 (8.8)	10,008 (8.4)
Unknown	11 (<0.1)	7 (<0.1)	2 (<0.1)
Ethnicity, n (%)			
White	99,736 (21.8)	90,175 (23.5)	35,867 (30.3)
Black	21,785 (4.8)	17,928 (4.7)	5778 (4.9)
Hispanic	25,765 (5.6)	21,562 (5.6)	6729 (5.7)
Asian/other	6424 (1.4)	5577 (1.5)	1822 (1.5)
Unknown	303,692 (66.4)	247,979 (64.7)	68,335 (57.7)
Insurance, n (%)			
Commercial	410,780 (89.8)	34,3301 (89.6)	103,004 (86.9)
MediCare	15,103 (3.3)	13,700 (3.6)	7667 (6.5)
MediCaid	25,408 (5.6)	21,317 (5.6)	6435 (5.4)
Other/unknown	6111 (1.3)	4903 (1.3)	1425 (1.2)
Region, n (%)			
West	113,102 (24.7)	97,182 (25.4)	30,899 (26.1)
Midwest	64,608 (14.1)	56,284 (14.7)	18,242 (15.4)
Northeast	98,538 (21.5)	83,774 (21.9)	24,320 (20.5)
South	180,924 (39.6)	145,817 (38.1)	45001 (38)
Unknown	230 (0.1)	164 (<0.1)	69 (0.1)
PrEP use, n (%)			
Naive user[a]	145,127 (31.7)	113,585 (29.6)	28,536 (24.1)
Experienced user	312,275 (68.3)	269,636 (70.4)	89,995 (75.9)
Prior renal disease,[b] n (%)	26,523 (5.8)	24,091 (6.3)	12,733 (10.7)
Prior liver dysfunction,[b] n (%)	21,390 (4.7)	19,599 (5.1)	9284 (7.8)

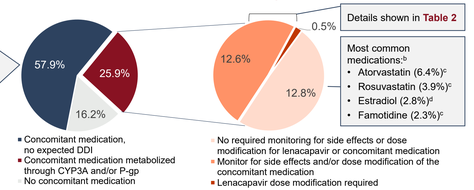
[a]Defined as no prior use of PrEP before the first prescription in 2024. [b]Diagnosed prior to filled date of first PrEP prescription in 2024.

DDI, drug-drug interaction; PrEP, pre-exposure prophylaxis.

Concomitant Medication Use

- Most (83.8%) PrEP users were taking at least one concomitant medication in 2024 (**Table 1**)
- In total, 25.9% PrEP users had concomitant use of at least one medication metabolized through CYP3A and/or P-gp (**Table 1**)
- If lenacapavir were used in place of the current PrEP option, 0.5% of all PrEP users in 2024 would have required lenacapavir dose modification and 12.6% would have required monitoring for side effects or consideration of dose modification of the concomitant medication (**Figure 2**)
  - No monitoring for side effects or dose modification of either medication would have been required for the remaining 12.8% of PrEP users with potential DDIs

Figure 2. Concomitant Medication Use and Potential DDIs[a] With Lenacapavir



[a]Defined here as medications metabolized through CYP3A and/or G-pg. [b]Includes all medication users; not mutually exclusive. [c]No clinically significant interaction per the US product label.[1] [d]No clinically significant interaction found in prior study.[5]

DDI, drug-drug interaction; PrEP, pre-exposure prophylaxis.

Medication With Lenacapavir DDIs

- The most common concomitant medications requiring lenacapavir dose modifications were oxcarbazepine (0.3% of all PrEP users), carbamazepine (0.1%) and rifampin (<0.1%) (**Table 2**)
- The most common medications requiring monitoring with potential dosage change were erectile dysfunction medications (10.7%), e.g., tadalafil (7.5%), sildenafil (4.1%), and vardenafil (0.1%) (individuals may have received more than one ED medication; **Table 2**)

Table 2. Concomitant Medications Requiring Dose Modification or Monitoring[a]

DDI category	Drug class	Indication	N	Proportion of all PrEP users (%)	Mean duration (days)	Prescription fills (n)
Lenacapavir dose modification (all)			**2433**	**0.53**	**125**	**4**
Oxcarbazepine	Anticonvulsant	Seizure disorders, nerve pain,[b] bipolar disorder[b]	1502	0.33	132	4
Carbamazepine			465	0.10	144	4
Phenytoin			117	0.03	142	4
Phenobarbital			101	0.02	102	4
Rifampin	Antibacterial	Bacterial infections (including tuberculosis)	193	0.04	58	2
Rifabutin			43	0.01	18	1
Rifapentine			28	0.01	62	2
Enzalutamide	Antiandrogen	Prostate cancer	8	<0.01	145	6
Apalutamide			6	<0.01	118	5
Monitoring for side effects or dose modification of concomitant medication (all)			**57,736**	**12.62**	**113**	**4**
Tadalafil for ED (>2.5 mg/day)	Vasodilator (PDE5 inhibitor)	Erectile dysfunction, pulmonary arterial hypertension[d]	34,082	7.45	134	4
Taladafil for PAH[c]			405	0.09	87	3
Sildenafil for ED (>25 mg/day)			18,603	4.07	79	3
Sildenafil for PAH			4331	0.95	79	3
Vardenafil (>5 mg/day)			328	0.07	52	3
Simvastatin (>10 mg/day)	Statin	High cholesterol and triglycerides	2407	0.53	200	4
Lovastatin (>20 mg/day)			155	0.03	204	4
Dexamethasone	Corticosteroid	Inflammation, immune overactivity	2038	0.45	9	1
Hydrocortisone/cortisone			323	0.07	127	3
Rivaroxaban	Anticoagulant	Prevent/treat blood clots	1362	0.30	167	4
Warfarin			513	0.11	216	5
Dabigatran			55	0.01	167	4
Edoxaban			2	<0.01	195	4
Triazolam	Sedative	Insomnia	555	0.12	18	2
Midazolam		Anesthesia, seizure management	82	0.02	27	2
Digoxin	Antiarrhythmic	Heart failure, atrial fibrillation	111	0.02	158	3
Dihydroergotamine[e]	Ergot derivative	Migraine and cluster headaches	28	0.01	79	3
Ergotamine[e]			5	<0.01	62	3
No interaction expected and no dose adjustments needed (all)[f]			**58,362**	**12.8%**	**141**	**3**

Proportion of PrEP users: ≤0.10% >0.10 to 1.00% >1.00%

[a]Numbers listed for each medication include all individuals taking the specific medication, regardless of their assigned DDI level, and are not mutually exclusive. [b]Oxcarbazepine and carbamazepine only. [c]Not recommended in combination with lenacapavir per US and EU product labels. [d]Sildenafil and vardenafil only. [e]Not recommended in combination with lenacapavir per US product label. [f]Includes the following: atorvastatin, rosuvastatin, estradiol, famotidine, progestins, sildenafil (ED; ≤25 mg/day), pravastatin, tadalafil (ED; ≤2.5 mg/day), norethisterone enanthate, medroxyprogesterone acetate, simvastatin (≤10 mg/day), ethinylestradiol, bicalutamide, etonogestrel, itraconazole, enoxaparin, lovastatin (≤20 mg/day), ketoconazole, vardenafil (≤5mg/day), pitavastatin, fluvastatin, voriconazole, darolutamide.

ED, erectile dysfunction; DDI, drug-drug interaction; PAH, pulmonary arterial hypertension; PDE5, phosphodiesterase Type 5; PrEP, pre-exposure prophylaxis.

Limitations

- This analysis may not have captured every sensitive substrate, as some may not have been included in the initial lists used in this study
- Tadalafil for PAH, dihydroergotamine, and ergotamine are not recommended for use in combination with lenacapavir but were included in recognition that co-administration may still occur in certain clinical situations
- These data may underestimate concomitant medication usage if individuals received treatment outside their insurance plan or at a health system that does not contribute to the dataset, including over-the-counter medications and supplements not captured in the pharmacy database
- This is a descriptive analysis based on adjudicated pharmacy claims. Clinical decisions and actions to mitigate DDIs are not reflected and remain the responsibilities of the treating healthcare provider