

PrEP: A Reference Guide on Less Common Scenarios

1. Inconclusive HIV Test While on PrEP

What an inconclusive HIV test could mean:

- Early HIV infection
- A false positive test

There is evidence that, in acute infection, PrEP can blunt the HIV antibody response, with either nonreactive or atypical HIV serology in a setting where viral load is likely to be undetectable.

2. Steps if HIV Ag/Ab Test Is Positive While on PrEP

A. For People Receiving Oral PrEP

Perform HIV 1/2 differentiation assay if HIV Ag/Ab test is positive



Perform quantitative HIV RNA testing to measure HIV viral load (even if differentiation assay is negative or indeterminate) and repeat HIV Ag/Ab test



Is new HIV infection likely?

eg, poor adherence to PrEP, symptoms of acute HIV infection



Assume that infection is real

Intensify ART while investigations are ongoing

Continue TDF/FTC and add a 3rd agent with a high barrier to resistance such as dolutegravir (or replace TDF/FTC with TLD) while awaiting viral load testing (Disadvantage: might make a definitive result more difficult)



Is new HIV infection unlikely?

eg, optimal adherence, no recent exposures



Continue TDF/FTC PrEP while awaiting results of viral load testing (Disadvantage: can drive emergence of resistance if seroconverting)

Subsequent approach to treatment depends on results of viral load testing:

If testing results are concordant with acute HIV infection (positive Ag/Ab test and high viral load), continue the HIV treatment regimen and add an integrase inhibitor with a high barrier to resistance, if not started already.

Most people will suppress their HIV viral load on this regimen, even if there is resistance to TDF or FTC.

If testing results are discordant with acute HIV infection (positive Ag/Ab test with a negative or very low HIV viral load [eg <100 copies/mL]), the subsequent treatment approach is less clear, and such cases should be managed in consultation with an HIV specialist.

1. If index of suspicion of acute HIV infection is high, continue ART treatment, but more sensitive testing for occult HIV may be required depending on what is available locally (eg HIV Proviral DNA, Western blot).
2. Stopping oral PrEP for 1-2 weeks is an option (not an option for LA CAB); this allows HIV replication in the absence of drug pressure and HIV Ag/Ab are more likely to detect virus; however this carries a risk of HIV acquisition if they have not actually seroconverted.

B. For People Receiving LA CAB

The diagnosis of HIV may be delayed due to the suppression of the HIV virus by LA CAB, resulting in false negative HIV tests. This is known as the long-acting early viral inhibition (LEVI) syndrome.

If HIV test is ambiguous, it may be necessary to pause LA CAB injections by 1-2 weeks to allow HIV tests to be able to detect HIV acquisition.

If seroconversion occurs while receiving LA CAB, initiate ART with a PI-based regimen (eg darunavir/ritonavir) and send HIV resistance test concurrently. If the resistance test shows no integrase resistance, can switch to TLD.

References:

bashh.org/_userfiles/pages/files/draft_bashh_bhiva_prep_guidelines_240924_v30_final.pdf.
cdc.gov/hivnexus/hcp/prep/index.html.
iris.who.int/bitstream/handle/10665/378164/9789240097230-eng.pdf?sequence=1.

3. Managing Missed PrEP Doses

A. For People Receiving Oral PrEP

HIV Acquisition	Gap Between Last PrEP Dose Before Exposure and Resumption of PrEP	Recommendation After Exposure
Condomless anal sex (insertive/receptive) or insertive vaginal sex	≤7 days since last oral PrEP dose	Resume PrEP with a double dose as prescribed
	>7 days since last oral PrEP dose	Take double dose of PrEP as soon as possible in the 24 hours after exposure and continue daily; seek urgent advice from clinical services for intensification of post-exposure prophylaxis (PEP)
Receptive vaginal sex	≤3 days since last oral PrEP dose	Resume PrEP with a double dose as prescribed
	>3 days since last oral PrEP dose	Take double dose of PrEP as soon as possible in the 24 hours after exposure and continue daily; seek urgent advice from clinical services for intensification of PEP
Missed postcoital dose for on-demand PrEP	1st postcoital dose is missed	1st <i>postcoital</i> dose can be taken up to 48 hours after sex, provided at least 1 <i>precoital</i> tablet was taken ≥2 hours before sex Take 2nd postcoital dose 24 hours after 1st to complete the course

bashh.org/_userfiles/pages/files/draft_bashh_bhiva_prep_guidelines_240924_v30_final.pdf.

Basis of recommendations:

- Effective drug levels associated with 90% reduction in risk are maintained for at least 7 days in both colorectal tissue and peripheral blood mononuclear cells (PBMC) once achieved
- Although PBMC are not impacted by gender, effective levels are only maintained for 2-3 days in the female genital tract (FGT), and it is reasonable to assume there is inadequate protection for the FGT at the portal of entry if the last pill was taken more than 3 days prior to exposure

B. For People Receiving LA CAB

Unplanned missed injections (or following oral PrEP to replace an injection):

How much time has passed since the missed target injection date?

If ≤4 weeks since target injection date:

- Resume continuation injections as soon as possible
- Continue with every-2-month dosing schedule thereafter

If ≥4 weeks since target injection date:

- Repeat initiation injections (2 injections, 1 month apart)
- Continue with every-2-month dosing schedule thereafter

Planned missed injections (oral PrEP bridging):

- If a person plans to miss their target injection date by >7 days, daily oral CAB can be prescribed to bridge the gap between injections
- Daily oral CAB (30 mg) for up to 2 months
- Start oral CAB on the target injection date and continue daily until able to return
- When the person returns, apply the same dosing schedule as above:

If ≤4 weeks since target injection date:

- Resume injections as soon as possible
- Continue with every-2-month dosing schedule thereafter

If ≥4 weeks since target injection date:

- Repeat initiation injections (2 injections, 1 month apart)
- Continue with every-2-month dosing schedule thereafter

References:

Macdonald. S Afr J HIV Med. 2025;26: a1713.
iris.who.int/bitstream/handle/10665/378164/9789240097230-eng.pdf?sequence=1.

