



Monitoring PrEP & Addressing Complications - Part 2

JANET CABRALES, PHARMD, BCPS, AAHIVP

LCDR US PUBLIC HEALTH SERVICE

HCV/HIV CLINICAL PHARMACIST

PHOENIX INDIAN MEDICAL CENTER

JANET.CIFUENTES@IHS.GOV

Objectives

- Know what biochemical parameters to monitor for people on PrEP
 - Lab monitoring
- Know what patient factors to monitor for people on PrEP
 - Side effects of medication
 - Adherence
- Know how and when to consider transitioning from non-occupational **post**-exposure prophylaxis (nPEP) to **pre**-exposure prophylaxis (PrEP)
- Know when to stop PrEP

New Guidelines!

Additions/Changes include:

Guideline:

Numerous changes, including info on Descovy for PrEP, cabotegravir for PrEP (in expectation of FDA approval for PrEP **on/about 1/24/22**), 2-1-1 dosing, Same-day PrEP starts, telemedicine, and revised lab monitoring recommendations, and many more

Supplement:

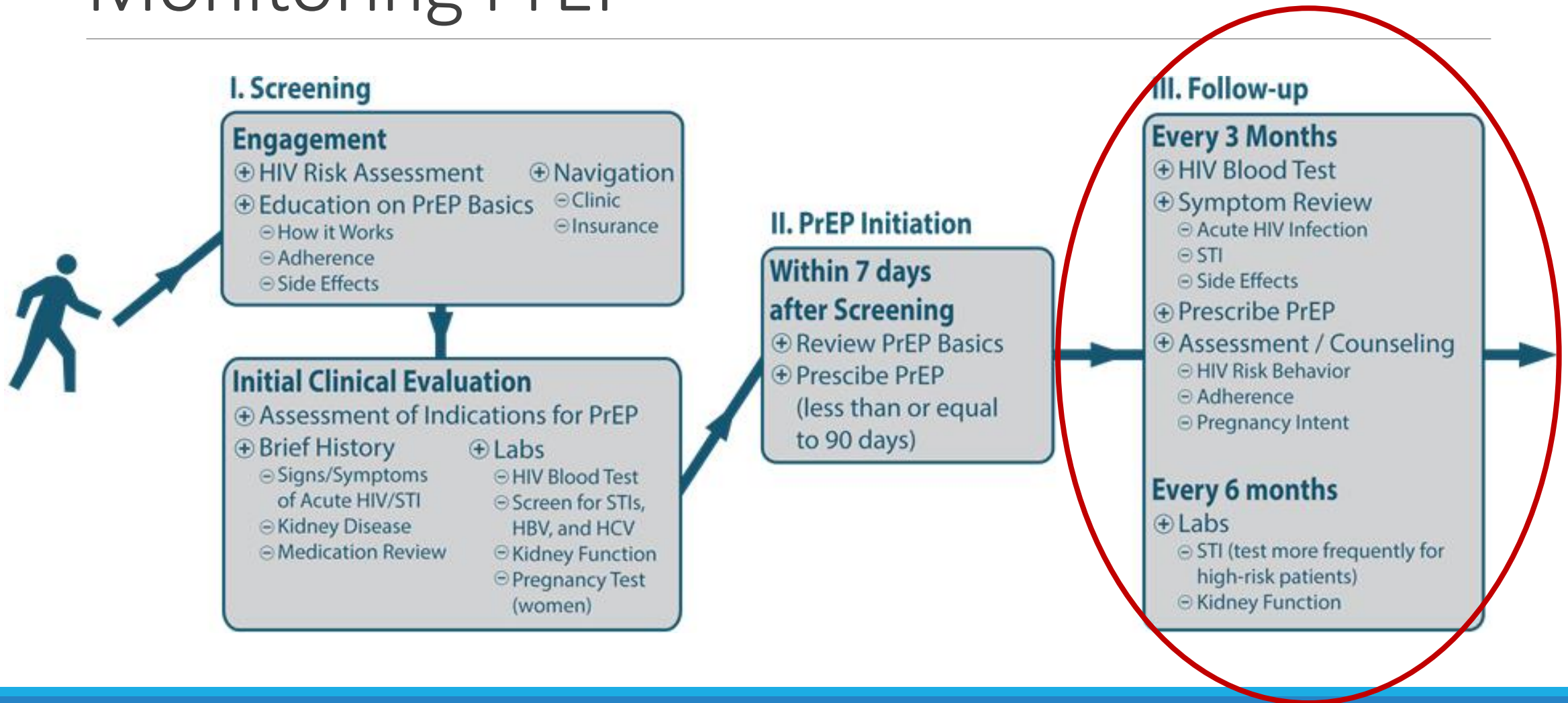
- Checklist updated to include Descovy , 2-1-1 Truvada for MSM, and cabotegravir
- Added information about Descovy to Patient Information Sheet about Truvada
- Added a Patient Information Sheet about cabotegravir
- Restored a revised section on risk reduction counseling for clinicians
- Text specific to cabotegravir was added to several sections.

**NEW PrEP GUIDELINES
OFFICIALLY RELEASED
12/8/21. BROWSER
SEARCH FOR “UPDATED
PREP GUIDELINES CDC”**

or

<https://www.cdc.gov/hiv/clinicians/prevention/prep.html>

Monitoring PrEP



Monitoring on PrEP

After 1st month:

- Call to follow up on new start, any lab results not yet given to patient
- Assess for side effects and address any adherence issues or questions
- Provide support for obtaining medication refills, as needed

At least every 3 months:

- Repeat HIV testing and assess for signs or symptoms of acute infection to document that patients are still HIV negative
- Repeat pregnancy testing for women who may become pregnant
- Provide a prescription or refill authorization of daily TDF/FTC (or FTC/TAF) for no more than 90 days
- Assess side effects, adherence, and HIV acquisition risk behaviors
- Provide support for medication adherence and risk-reduction behaviors
- Respond to new questions and provide any new information about PrEP
- Conduct STI testing for sexually active persons with signs or symptoms of infection and screening for asymptomatic MSM at high risk for recurrent bacterial STIs (e.g., those with syphilis, gonorrhea, or chlamydia at prior visits or multiple sex partners)

At least every 6 months:

- Monitor eCrCl for persons age ≥ 50 years or who have an eCrCl < 90 ml/min at PrEP initiation
- If other threats to renal safety are present (e.g., HTN, diabetes), renal function may require more frequent monitoring or may need to include additional tests (e.g., urinalysis for proteinuria)
- A rise in serum creatinine is not a reason to withhold treatment if eCrCl remains ≥ 60 ml/min for F/TDF or ≥ 30 ml/min for F/TAF.
- If eCrCl is declining steadily (but still ≥ 60 ml/min or ≥ 30 ml/min for F/TAF), consultation with a nephrologist or other evaluation of possible threats to renal health may be indicated.
- Conduct STI screening for sexually active persons, i.e., syphilis and gonorrhea for all PrEP patients and chlamydia for MSM and TGW even if asymptomatic

At least every 12 months:

- Monitor eCrCl for all patients continuing on PrEP medication
- Monitor triglycerides, cholesterol levels, and weight for patients on F/TAF
- Conduct chlamydia screening for heterosexual patients, even if asymptomatic

Quarterly Visits

Provide the following services:	
At 3 months after PrEP initiation:	<ul style="list-style-type: none">• Test for HIV.• Measure serum creatinine and estimate creatinine clearance.• Provide medication adherence and behavioral risk reduction support.• Additionally, for<ul style="list-style-type: none">◦ MSM: screen for bacterial STIs*;◦ Women with reproductive potential: test for pregnancy; and◦ PWID: assess access to sterile needles/syringes and to drug treatment services.
Every 3 months after the first 3-month follow-up:	<ul style="list-style-type: none">• Test for HIV.• Provide medication adherence and behavioral risk reduction support.• Additionally, for<ul style="list-style-type: none">◦ MSM: screen for bacterial STIs*;◦ Women with reproductive potential: test for pregnancy; and◦ PWID: assess access to sterile needles/syringes and to substance use disorder treatment services.
Every 6 months after the first 3-month follow-up:	<ul style="list-style-type: none">• Measure serum creatinine and estimate creatinine clearance.• For all sexually active patients: Screen for bacterial STIs*.

Monitoring Oral PrEP Labs

Test	Screening/Baseline Visit	Q 3 months	Q 6 months	Q 12 months	When stopping PrEP
HIV Test	X*	X			X*
eCrCl	X		If age ≥ 50 or eCrCL < 90 ml/min at PrEP initiation	If age < 50 and eCrCl ≥ 90 ml/min at PrEP initiation	X
Syphilis	X	MSM /TGW	X		MSM/TGW
Gonorrhea	X	MSM /TGW	X		MSM /TGW
Chlamydia	X	MSM /TGW	X		MSM /TGW
Lipid panel (F/TAF)	X			X	
Hep B serology	X				
Hep C serology	MSM, TGW, and PWID only			MSM, TGW, and PWID only	

Table 5, page 44 of new Guidelines

* Assess for acute HIV infection (see Figure 4)

Lab Monitoring – MAJOR update

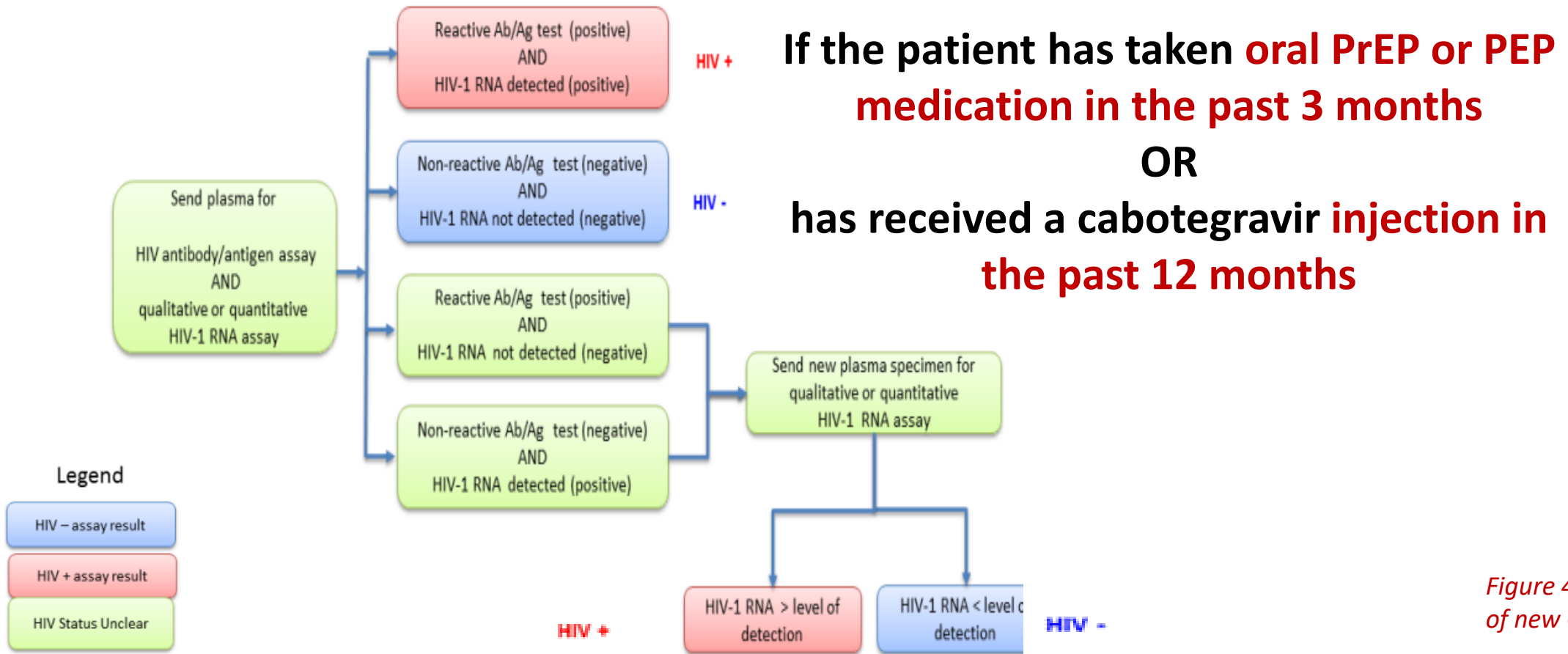


Figure 4b, page 31 of new Guidelines

New Start HIV Serology

If the patient has NOT taken oral PrEP or PEP medication in the past 3 months AND has NOT received a cabotegravir injection in the past 12 months

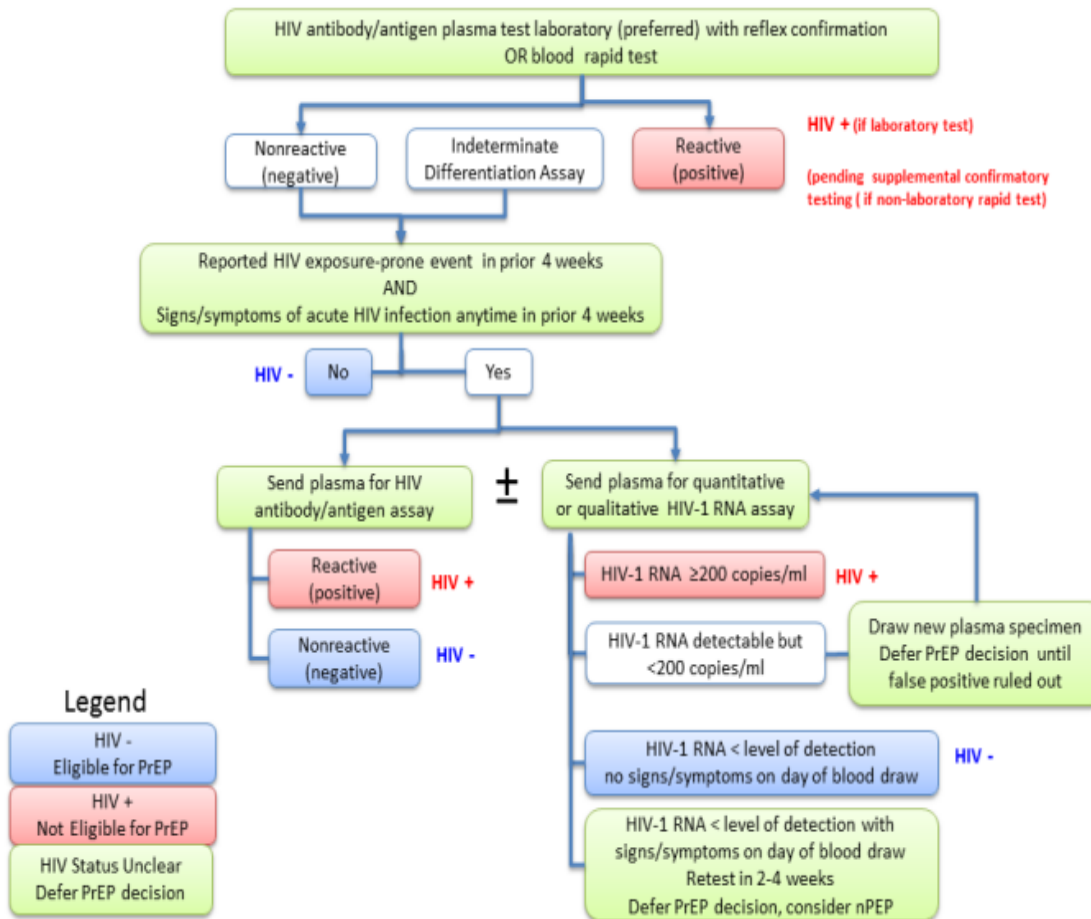


Figure 4a, page 30 of new Guidelines

A Bit More on HIV Serology

- Requires a negative antigen antibody test in the previous 7 days before starting PrEP in patients who are PrEP naïve or off PrEP > 3 months
- Requires a negative antigen/antibody screen AND a negative HIV RNA with continuation or restart after a period of non-adherence lasting less than 3 months (oral PrEP)
- A high index of suspicion for Acute HIV when assessing current HIV status
 - High-risk encounter in past month + signs/symptoms of acute HIV?
 - Does the person on PrEP have poor adherence?
 - Does the person on PrEP have elevated risk?
 - Presence of STIs, known exposure to HIV + partner
 - Does the person on PrEP have clinical indicia of acute HIV (even without reported high-risk encounter)?

Perform an HIV RNA test if concern for acute HIV

- Positive HIV serology (4th gen) is confirmed with:
 - HIV 1/2 antibody differentiation test
 - HIV RNA test (either a viral load or a qualitative HIV RNA)

CLINICIANS CAN CALL THE NATIONAL CLINICIANS CONSULTATION CENTER PREPLINE AT 855-448-7737 FOR ADVICE ABOUT INTERPRETATION OF HIV TEST RESULTS AND MANAGEMENT OF PATIENTS WHO ACQUIRE HIV INFECTION WHILE TAKING PREP MEDICATION.

STI testing

- Refer to Dr. Iralu's comprehensive presentation from last session
- Symptoms consistent with common STIs include urethral discharge, dysuria, ulcers, rash, lymphadenopathy, and anorectal symptoms that might be consistent with proctitis (e.g., discharge, rectal bleeding, pain on defecation, or pain during anal sex)
- Approximately 70% of gonococcal and chlamydial infections might be missed if urogenital-only testing is performed among MSM
- Ulcerative STIs such as herpes and syphilis can raise HIV acquisition risk by 2.5 times, and prompt treatment reduces that risk back to baseline
 - One in 20 MSM with a primary or secondary syphilis diagnosis were diagnosed with HIV within a year
 - MSM with rectal chlamydia and/or gonorrhea are almost three times more likely to get HIV within a year than MSM without a rectal infection
- Routine STI screening is part of PrEP monitoring
 - Opens a great opportunity for risk assessment/risk reduction discussion
 - Helps with recruitment-inquire about partners when an STI is documented, and offer partners PrEP
 - If partner is non-Native, refer to local PrEP navigators
 - <https://prelocator.org/>, PLUSH, MISTR

FTC/TDF (& FTC/TAF) Black Box Warning

BOXED WARNING: RISK OF DRUG RESISTANCE WITH USE OF F/TDF or F/TAF FOR PrEP IN UNDIAGNOSED EARLY HIV-1 INFECTION and POST TREATMENT ACUTE EXACERBATION OF HEPATITIS B

- FTC/TDF or FTC/TAF for PrEP must only be prescribed to individuals confirmed to be HIV-negative immediately prior to initiation and at least every 3 months during use. Drug-resistant HIV-1 variants have been identified with use of TRUVADA FOR PrEP following undetected acute HIV-1 infection. Do not initiate if signs or symptoms of acute HIV-1 infection are present unless HIV-negative status is confirmed
- Severe acute exacerbations of hepatitis B have been reported in HBV-infected patients who discontinued TRUVADA. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients with HBV after discontinuing TRUVADA. If appropriate, initiation of anti-hepatitis B therapy may be warranted

Monitoring in Patients with HBV

- PrEP should not be withheld while awaiting HBV serology results
- Test for HBV DNA with a quantitative assay to determine the level of HBV replication at the time PrEP is prescribed, or as soon as positive result is received (ideally before patient has been on PrEP for very long)
- All persons screened for PrEP who test positive for hepatitis B surface antigen (HBsAg) should be evaluated by a clinician experienced in HBV treatment
 - For clinicians without this experience, co-management with an infectious disease or a hepatic disease specialist should be considered
- Reinforce the need for adherence to prevent reactivation of HBV infection

Monitoring Differences

Monitor weight, triglyceride, and LDL at baseline and q 12 months for patients on F/TAF (not needed for F/TDF)

Updated guideline states that there is no need to switch from F/TDF to F/TAF for most patients. While incremental differences in lab markers of bone metabolism and renal function have been seen in some studies, no differences in clinically meaningful adverse events have been seen

TRUVADA	DESCOVY
<p>Safety: general</p> <p>Both medicines have very low rates of side effects overall. Some people experience “start-up” symptoms including diarrhea, nausea and vomiting, which usually resolve in the first three months of PrEP use.</p>	<p>Safety: general</p> <p>Both medicines have very low rates of side effects overall. Some people experience “start-up” symptoms including diarrhea, nausea and vomiting, which usually resolve in the first three months of PrEP use.</p>
<p>Bone health</p> <p>People with osteoporosis should avoid</p>	<p>Bone health</p> <p>Safer to take for people with osteoporosis</p>
<p>Kidney health</p> <p>People with kidney issues or a strong family history of kidney disease should avoid</p>	<p>Kidney health</p> <p>Safer to take for people with kidney issues or a strong family history of kidney disease, though monitoring still recommended</p>
<p>Weight loss/gain</p> <p>May cause a small degree of weight loss¹</p>	<p>Weight loss/gain</p> <p>May cause a small degree of weight gain²</p>
<p>Cholesterol</p> <p>May cause small decreases in HDL, LDL and total cholesterol¹</p>	<p>Cholesterol</p> <p>May cause small increases in LDL cholesterol and triglycerides^{2,3}</p>

Kidney Health

- DISCOVER: No difference in clinically important renal health measures b/w men taking F/TDF or F/TAF
 - Changes seen in markers of proximal tubular function that favored F/TAF
 - Possible longer-term safety benefit of prescribing F/TAF for men with pre-existing risk factors for renal dysfunction (DM, HTN)
- In persons with HIV prescribed TDF-containing regimens, mild decreases in renal function have been documented, and occasional cases of acute renal failure, including Fanconi's syndrome, have occurred
 - More likely in pts >50 years of age or w/ a eCrCl <90 ml/min at PrEP start with F/TDF
 - Typically reversed when PrEP was discontinued
- In the single clinical trial of F/TAF for PrEP among MSM (+ small # TGW), no decrease in renal function was observed

•F/TDF: ≥ 60 ml/min
•F/TAF: ≥ 30 ml/min
•CAB: *Will be only PrEP option for patients on dialysis or eCrCl <30 ml/min*

Cardiovascular Health

- DISCOVER clinical trial compared F/TDF and F/TAF for PrEP in MSM and TGW
 - F/TDF:
 - Associated with reductions in HDL and LDL cholesterol
 - F/TAF:
 - Higher rates of triglyceride elevation
 - Higher rates of weight gain
- May indicate a longer-term safety **risk** when prescribing F/TAF PrEP for men with pre-existing cardiovascular health risk factors (e.g., obesity, age, lipid profiles)
- All persons prescribed F/TAF for PrEP should have monitoring of triglyceride and cholesterol levels every 12 months
- Lipid-lowering medications should be prescribed when indicated

Bone Health

- iPrEx trial (F/TDF) and the CDC PrEP safety trial in MSM (F/TDF) conducted DEXA scans on subset of MSM & determined that a small (~1%) decline in BMD that occurred during the first few months of PrEP either stabilized or returned to normal
- DEXA substudy of Discover trial men randomized to F/TAF showed slight mean percentage increases in BMD at the hip and spine through 96 weeks of observation, while men randomized to F/TDF showed mild decreases at both anatomic sites
- **NO** increase in fragility (atraumatic) fractures over the 1-2 years of observation in these studies comparing those persons randomized to receive PrEP medication and those randomized to receive placebo
- DEXA scans or other assessments of bone health are not recommended before the initiation of PrEP or for the monitoring of persons while taking PrEP
- BUT... any person being considered for PrEP who has a history of pathologic or fragility bone fractures or who has significant risk factors for osteoporosis should be referred for appropriate consultation and management

Liver Health

- AST/ALT/T.bili: while medications for PrEP RARELY cause liver problems, it must be kept in mind for people on PrEP with HBV history due to black box warning
- Most common cause of liver enzyme abnormality in PrEP clinic is unrelated liver problems (not PrEP)
- Alcohol can be responsible for increased risk for HIV acquisition with poor adherence and black-out-sex being 2 common issues
 - EtOH use/ SUDs are NOT a contraindication for PrEP
- **Revised guidelines state that liver function tests are not indicated routinely** for patients on either F/TDF or F/TAF for PrEP

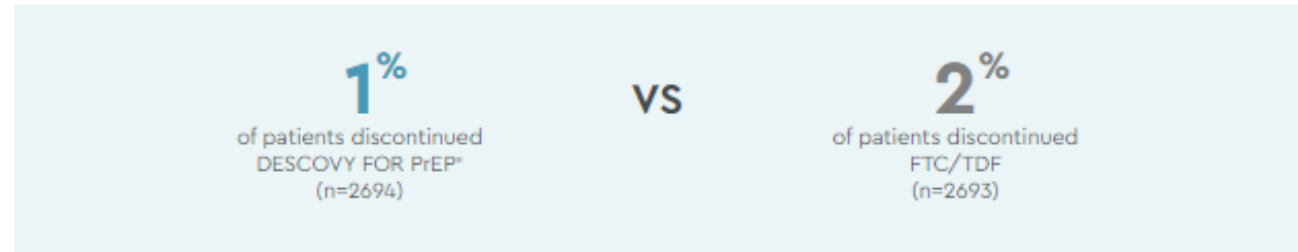
Adverse Events

Some (<10%) of patients prescribed F/TDF or F/TAF experience a “start-up syndrome” that usually resolves within the first month of taking PrEP medication:

- Headache, nausea, or abdominal discomfort
- Discuss use of over-the-counter medications should these temporary side effects occur
- Counsel on signs or symptoms that need urgent evaluation if they occur between visits (e.g., those suggesting possible acute renal injury or acute HIV infection)

Weight gain is a reported side effect of F/TAF for PrEP!
(the smaller pill can make you bigger...)

Few discontinuations due to adverse events



Adverse reactions (all grades) reported in ≥2% of patients were similar in both study arms

	DESCOVY® (n=2694)	FTC/TDF (n=2693)
Diarrhea	5%	6%
Nausea	4%	5%
Headache	2%	2%
Fatigue	2%	3%
Abdominal pain	2%	3%

Mean change in lipid values^{2-4,a}

Lipid value	Target level	DESCOVY		FTC/TDF	
		Baseline (mg/dL)	Week 96 change	Baseline (mg/dL)	Week 96 change
Total cholesterol (fasted)	<200 mg/dL	175	-2	176	-13
HDL cholesterol (fasted)	≥60 mg/dL	51	-2	51	-4
LDL cholesterol (fasted)	<100 mg/dL	103	-1	103	-8
Triglycerides (fasted)	<150 mg/dL	108	+6	111	-7
Total-cholesterol-to-HDL ratio	<4.5	3.7	+0.1	3.7	0.0

PrEP Adherence is Critical

92%-99% reduction in those with good adherence (PWID = 74% +)

- 7 PrEP pills per week -> 99% est. protection
- 4 PrEP pills per week -> 96% est. protection
- 2 PrEP pills per week -> 76% est. protection

Lab study strongly suggests that there is less “forgiveness” for missed doses among women than among MSM

Figure 5: Adherence and F/TDF PrEP Efficacy in MSM

Weekly Medication Adherence Estimated by Drug Concentration	HIV Incidence per 100 person/years
None	4.2
≤2 pills/week	2.3
2-3 pills/week	0.6
≥4 pills/week	0.0

NOTE: Lab monitoring of drug levels not typically utilized – no reference ranges or approved point-of-care tests

Adherence Check-Ins

Box B: Key Components of Oral Medication Adherence Counseling

Establish trust and bidirectional communication

Provide simple explanations and education

- Medication dosage and schedule
- Management of common side effects
- Relationship of adherence to the efficacy of PrEP
- Signs and symptoms of acute HIV infection and recommended actions

Support adherence

- Tailor daily dose to patient's daily routine
- Identify reminders and devices to minimize forgetting doses
- Identify and address barriers to adherence
- Reinforce benefit relative to uncommon harms

Monitor medication adherence in a non-judgmental manner

- Normalize occasional missed doses, while ensuring patient understands importance of daily dosing for optimal protection
- Reinforce success
- Identify factors interfering with adherence and plan with patient to address them
- Assess side effects and plan how to manage them

A brief medication adherence question

“Many people find it difficult to take a medicine every day.

Thinking about the last week; on how many days have you **not** taken your medicine?”

Post-Exposure Prophylaxis (nPEP) to Pre-Exposure Prophylaxis (PrEP)

Two types of patients may be candidates for PrEP use after post-exposure prophylaxis (nPEP):

- Patients who request PrEP and also have had a possible sexual or injection drug-related HIV exposure in the prior 72 hours (i.e., are within the recommended window to start nPEP)
- Patients who request repeated courses of nPEP, particularly over a relatively recent period (e.g., more than twice during the past 6 months)

Discuss transition from nPEP x 28 days to PrEP (without a break in meds) and repeat HIV screen in 4 weeks if patient meets PrEP criteria and is willing to fulfill monitoring requirements

- Discuss PrEP with patient at initial nPEP visit, if appropriate
- Follow up with patient a few days after start of nPEP to assess adherence and tolerability
- Have patient RTC for repeat HIV screen and PrEP discussion just prior to completion of nPEP
- If no suspicion of acute HIV, complete any outstanding baseline PrEP labs
 - If suspicion of acute HIV, continue nPEP regimen pending confirmation of patient's HIV status
- Dispense (or have plan to acquire) PrEP med by the time nPEP runs out to avoid break in meds
- Schedule follow up visits and labs before patient leaves visit

Discontinuation of PrEP

- Patient choice
- Intolerable toxicities
- Life situation changes resulting in lower risk of HIV acquisition
- Chronic nonadherence to prescribed dosing or monitoring regimen
- Acquisition of HIV

Upon discontinuation, document the following in the health record:

- Reason for discontinuation
- HIV status at the time of discontinuation
- Recent medication adherence and reported sexual risk behavior

Lowered Risk

- **U=U:** PrEP may no longer be necessary if partner with known HIV is undetectable on meds
 - However, if patient wants to remain on PrEP after being counseled on U=U, do not d/c
- Person on PrEP in committed relationship with partner(s) who all do testing together
- Person on PrEP no longer engages in unprotected sex or needle sharing
- Person on PrEP choosing low risk behaviors such as oral only
- Person on PrEP committing to consistent and correct condom use

Seroconversion

When an HIV test during a follow-up visit indicates possible infection on PrEP pt:

- Counsel the patient about their HIV status and the resulting management plan
- Conduct confirmatory HIV testing and supplemental tests (i.e. new HIV lab panel), if indicated
- Convert the PrEP regimen to an HIV treatment regimen recommended by the DHHS guidelines
 - It is not necessary to stop antiretrovirals entirely while waiting for additional laboratory test results. In the event that the patient has HIV infection, immediate initiation of HIV treatment is indicated
- Provide client education about time to viral load suppression and treatment as prevention
- Consult with and transfer care to an experienced HIV care provider, if necessary
- Schedule follow-up visits, including social services, if required
- Complete an HIV case report for the health department, including PrEP use info

Expanded Services

		MSM	MSW*	Women*	PWID
Vaccines# (if not previously vaccinated)	Hepatitis A vaccine	Yes	Yes	Yes	Yes
	Hepatitis B vaccine	Yes	Yes	Yes	Yes
	HPV vaccine	Through age 26	Through age 26	Through age 26	Through age 26
	Meningococcal B vaccine	Ages 16-18	Ages 16-18	Ages 16-18	Ages 16-18
	Influenza vaccine	Yes	Yes	Yes	Yes
General Health	Hepatitis C infection [^]	Ages 18-79	Ages 18-79	Ages 18-79	Ages 18-79
	Screen for depression [^]	Yes	Yes	Yes	Yes
	Screen for unhealthy alcohol use [^]	Ages 18 and older	Ages 18 and older	Ages 18 and older	Ages 18 and older
	Screen for smoking [^]	Yes	Yes	Yes	Yes
	Screen for Intimate Partner Violence [^]	Yes		Yes	If female, Yes
Women's Health	Mammography [^]			Ages 50-74 every two years	If female, Ages 50-74 every two years
	Screen for cervical cancer ^{^~}			Ages 21-65 every three years	If female, Ages 21-65 every three years
Men's Health	Screen for prostate cancer [^]	Ages 55-69	Ages 55-69		If male, Ages 55-69

Table 8, page 64 of new Guidelines

References

- Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 Update: a clinical practice guideline. <https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf>. Published December 2021.
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