

Providing HIV Pre-Exposure Prophylaxis (PrEP): Protocol¹ for Edison Clinic

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¹ Adapted from CDC's "Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 Clinical Practice Guideline"

DEFINITIONS

- **HIV PrEP:** Use of antiretroviral medication in an HIV-negative person before HIV exposure to prevent HIV acquisition
 - Truvada is the only FDA-approved medication for HIV PrEP.
- **HIV post-exposure prophylaxis (PEP):** Use of antiretroviral medication after an isolated HIV exposure or high-risk event in an attempt to stop HIV replication and establishment of infection
 - PEP must be started as soon as possible to be effective and always within 72 hours of the possible exposure.

INDICATIONS FOR PrEP

HIV-negative adult (≥ 18 years of age) and *any* of the following:

- in an ongoing relationship with an HIV-positive partner
- MSM or transgender woman who has had anal sex without a condom or been diagnosed with any sexually transmitted infection (STI) in the past 6 months by lab testing or self-report
- man or woman who does not regularly use condoms during vaginal or anal sex and has a partner or partners who are IDU, transgender, or MSM
- injected drugs not prescribed by a clinician in the past 6 months and either shared drug preparation equipment in the past 6 months or been in a methadone, buprenorphine, or suboxone treatment program in the past 6 months
- PEP use twice or more in the past year

CONTRAINDICATIONS

- Estimated creatinine clearance (eCrCl) < 60 mL/min
- HIV infection, documented or suspected

PRECAUTIONS

- Hepatitis B infection
- History of pathologic or fragility bone fractures
- Significant risk factors for osteoporosis
 - In any of these cases, refer for appropriate consultation and management.
- Age < 18 years
 - PrEP safety and effectiveness have not been studied in persons < 18 years of age.
 - In California, youth 12 years and older may consent to STD prevention services.
- Periconception and pregnant or breastfeeding women
 - Refer to CDC's "Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 Clinical Practice Guideline" for guidance.

INITIAL PROVIDER VISIT

HIV RISK ASSESSMENT

- Sexual history
 - Consider utilizing the “Infectious Disease > STI - Sexual History” HPI template.
 - Consider utilizing the “MSM Risk Index” tool. (See pp 20-21 of the “Clinical Providers’ Supplement” of the CDC PrEP Clinical Guidelines.)
 - <http://www.cdc.gov/hiv/pdf/PrEPProviderSupplement2014.pdf>
- Substance use history, with specific queries of IDU and, for MSM, crystal meth use
- HIV exposure or high-risk event within the past 72 hours
 - Consider immediate PEP followed by a seamless transition to PrEP if indicated
 - Contact UCSF Clinician Consultation Center at (888) 448-4911 if in need of case-by-case expert PEP consultation
 - <http://nccc.ucsf.edu/clinician-consultation/post-exposure-prophylaxis-pep/>
 - Consult the medical director in real-time with any questions regarding the logistics of PEP initiation including urgent access to medications

MEDICAL HISTORY

- Inquire specifically about any history of:
 - kidney disease
 - liver disease
 - Inquire specifically about chronic hepatitis B infection.
 - bone disease
 - osteoporosis
 - pathologic or fragility bone fractures

CONCOMITANT MEDICATIONS

- Document an accurate medication list with special attention to NSAIDs.

ACUTE RETROVIRAL SYNDROME ASSESSMENT

- Inquire about the presence of fever, fatigue, myalgia, rash, headache, sore throat, cervical adenopathy, arthralgia, night sweats, or diarrhea *within the past month*.
 - If acute or recent HIV infection is suspected, order an HIV RNA test.

STI SYMPTOM ASSESSMENT

- Inquire about the presence of dysuria, discharge, anorectal itching or pain, rash, or ulcers.
 - Test and treat appropriately.

LABS TO ORDER

- Select appropriate assessment and ICD-10 code: “High-risk sexual behavior” (Z72.51) and/or “HIV exposure” (Z20.6) and/or “Preventive medication therapy needed” (Z41.8)
 - REQUIRED LABS
 - HIV antibody
 - HIV RNA if there is clinical suspicion for acute retroviral syndrome
 - Serum creatinine (ensure weight is documented for calculation of eCrCl)
 - HBsAg (if not done within the past three months)
 - POC pregnancy test for women not known to be pregnant
 - RECOMMENDED LABS
 - Syphilis EIA
 - GC/CT urine
 - GC/CT rectal and pharyngeal for MSM
 - Provider or patient to collect specimens
 - HCV antibody (risk-based screening)
 - LABS TO CONSIDER
 - HBsAb (if considering HBV IZ)
 - HBcAb (to rule out occult HBV infection)
 - HAV IgG (if considering HAV IZ)

COUNSELING

- Daily adherence
 - Efficacy
 - Missed doses
 - Resistance
 - Notify provider and need for HIV testing prior to restarting PrEP if stopped for seven or more days
- Potential side effects
 - Truvada start-up syndrome with possible symptoms including:
 - Nausea
 - Abdominal upset
 - Loose stools
 - Flatulence
 - Headache
 - Most symptoms, if they occur, are mild and resolve within a few days to a few weeks
 - Renal toxicity
 - Bone mineral density loss
- Other prevention strategies
 - Condom use

- Contraception
 - Refer to PCP or OB/GYN as appropriate
- Time to achieving protection
 - Rectal: seven days
 - Vaginal: 20 days
- Symptom reporting
 - Notify triage immediately of symptoms of acute retroviral syndrome or STIs
 - Refer to educational handout
- Sharing medication
 - PrEP is exclusively for personal use and should not be shared with others
- Follow-up expectations
 - Provider visit and labs at least every three months
 - Expect phone call upon provider's receipt of initial lab results
 - Prescription will be sent if okay to start PrEP
 - Inform Medi-Cal patients of requirement to use Alphascript Pharmacy
 - Mail-delivery service only
- Nursing staff to provide patient with educational handout

DOCUMENTATION

- Document that patient understands risks/benefits and appropriate use of PrEP. If any concerns, consider delaying initiation until concerns are resolved.

STARTING PrEP UPON RECEIPT OF SCREENING LAB RESULTS (TELEPHONE ENCOUNTER)

- Provider reviews lab results
 - To start PrEP:
 - HIV antibody and RNA, if ordered, must be nonreactive/not detected *within the past 10 days*
 - Repeat HIV antibody test if more than 10 days have elapsed and an RNA test was not ordered
 - Redraw RNA if < 50,000 copies/mL to rule out a false positive result
 - eCrCl must be ≥ 60 mL/min
 - Cockcroft-Gault equation:
<http://reference.medscape.com/calculator/creatinine-clearance-cockcroft-gault>
 - If < 60 mL/min, provider to follow up appropriately. Consider repeat testing
 - HBsAg must be negative and no evidence of occult HBV infection
 - If positive or evidence of occult HBV infection, refer to hepatology clinic
 - Refer to CDC's Clinical Practice Guidelines for any special concerns
 - <http://www.cdc.gov/hiv/pdf/PrEPguidelines2014.pdf>

- Follow up with other lab results appropriately. Do not wait for STI, HCV antibody, or other non-essential lab results to start PrEP.
- Provider to call patient to inform whether cleared to start PrEP
- If cleared, send e-rx via telephone encounter (to Alphascript Pharmacy for Medi-Cal patients) for Truvada #30 with two refills. Include in sig indication: “for PrEP”
 - Alphascript Pharmacy to submit prior authorization
- Order future monitoring labs via virtual visit in the same telephone encounter
 - HIV antibody
 - Serum creatinine
 - STI screening as indicated
 - Pharyngeal and rectal specimens to be collected at the next provider visit
 - ALT as indicated (if at risk for HCV and HCV antibody has already been checked)
- Forward telephone encounter to PSA and request to schedule a follow-up appointment with provider in three months and a nurse visit for labs two weeks prior to provider visit
 - *NOTE:* Consider HIV antibody testing four weeks after PrEP initiation to confirm HIV-negative status.
 - *NOTE:* Consider checking creatinine sooner than in three months if clinically indicated, e.g., in the setting of diabetes or uncontrolled hypertension.

QUARTERLY PROVIDER VISITS

ASSESSMENT

- Side effects, e.g., headache, nausea, loose stools, flatulence
 - Consider symptom management with OTC medications
- Acute HIV and STI symptoms
- Adherence
- HIV risk assessment and sexual history
- Desire to continue PrEP
- Changes to medical history
- Changes to medications
 - Acyclovir, valacyclovir, cidofovir, ganciclovir, valganciclovir, aminoglycosides, high-dose or multiple NSAIDs, or other drugs that reduce renal function or compete for active renal tubular secretion: Serum concentrations of these drugs and/or TDF may be increased. Monitor for dose-related renal toxicities.
- Contraception for women
 - Refer as appropriate
- Review lab results with patient
 - Refer to “HIV Testing” and “Creatinine Monitoring” section
- Symptom-directed physical exam
 - Ensure weight is documented for calculation of eCrCl
- POC pregnancy test for women who are not known to be pregnant

Rx

- Give HAV, HBV, or Twinrix IZ if indicated
- Provide up to 3 refills of Truvada #30 for PrEP

FUTURE LABS TO ORDER

- HIV antibody
- HIV RNA if there is clinical suspicion for acute retroviral syndrome
 - In this case, HIV antibody and HIV RNA should be checked the day of the visit. If nonreactive/not detected, reorder HIV antibody via a telephone encounter (virtual visit) as a future lab to be completed prior to the next quarterly provider visit
- Serum creatinine (See “Creatinine Monitoring” section for frequency of testing)
 - STI screening as indicated
 - *NOTE:* Pharyngeal and rectal specimens are not collected at nurse visits and must be collected during provider visits
- ALT as indicated (if at risk for HCV and HCV antibody has already been checked)

FOLLOW-UP

- Provider visit in three months (ensure before runs out of pills)
- Nurse visit for labs two weeks prior to provider visit

HIV TESTING AFTER PrEP INITIATION

- HIV antibody testing should be conducted at least every three months for patients taking PrEP.
- **An HIV RNA test should be ordered whenever there is clinical suspicion for acute retroviral syndrome.**
- **HIV testing should be conducted for patients who have stopped PrEP (whether held by clinician or by patient) for seven or more days prior to resuming PrEP.**
 - HIV antibody and RNA, if ordered, must be nonreactive/not detected *within the past 10 days* prior to restarting PrEP.
 - Repeat HIV antibody test if more than 10 days have elapsed and an RNA test was not ordered
 - Redraw RNA if < 50,000 copies/mL to rule out a false positive result
- While on PrEP, there must be a documented nonreactive HIV antibody (and negative RNA test, if ordered) *within one month*, preferably within two weeks, of providing refills.
- PrEP should be discontinued immediately upon documentation of HIV seroconversion. (See “Discontinuing PrEP” section.)

CREATININE MONITORING

- Creatinine should be checked at least every three to six months during PrEP use.

- Consider more frequent monitoring if clinically indicated, e.g., in the setting of diabetes or uncontrolled hypertension.
- If the eCrCl is < 60 mL/min, Truvada should be held immediately via a telephone encounter and the creatinine should be repeated in two to four weeks. **Include HIV antibody testing.**
 - If the rechecked eCrCl is \geq 60 mL/min and HIV antibody is nonreactive, PrEP may be restarted and creatinine should be rechecked again in one month.
- If the creatinine is > 1.5x baseline (but eCrCl is \geq 60 mL/min), initiate a telephone encounter and assess for any other potential causes of the creatinine elevation, e.g., dehydration, protein supplement use, new medications, and NSAIDs. **Advise patient to continue employing other prevention strategies as PrEP may need to be held.** Recheck creatinine in two weeks.
 - If the rechecked eCrCl is < 60 mL/min, Truvada should be held immediately via a telephone encounter.
 - Patients who want to be on PrEP but have sustained creatinine elevations > 1.5x baseline and/or eCrCl < 60 mL/min should be referred to a nephrologist.

REFILL POLICY

- HIV testing and creatinine monitoring are essential to safe PrEP provision.
- Lab testing should be completed two weeks prior to a follow-up visit with ample time (ten to fourteen days) for receipt of results.
- Refills should be provided *during a provider visit* when lab results can be reviewed.
 - Pharmacies may send automatic refill requests well in advance of patients' running out of pills. These requests should be denied as lab testing likely will not yet have occurred.
- No more than three refills at any given time should be provided.
- If a patient does not attend a provider visit, but has completed his/her labs as required and results are normal, one refill may be provided. The patient must reschedule and attend a provider visit for further refills. At the time of the provider visit, provide two refills and then resume a three-month refill and follow-up schedule.

DISCONTINUING PrEP

- By clinician
 - Sustained eCrCl < 60 mL/min (See "Creatinine monitoring" section)
 - HIV seroconversion
- By patient
 - Provide counseling on HIV risk reduction and education on safely restarting PrEP.
 - **Advise continued use of Truvada (as PEP) if there was a high-risk event within the last seven days and the patient had been adherent to PrEP.**
 - Continue for 28 days post-high-risk event
- Conduct HIV antibody testing four weeks after Truvada discontinuation for any reason other than seroconversion.

DOCUMENTATION

- Document the reason for PrEP discontinuation and the HIV status of the patient at the time of discontinuation.
- Document counseling of other prevention strategies.

CLINICIAN DISCRETION

Individual patient factors may require clinician discretion in medical decision-making and, as such, divergences from this protocol may be necessary, especially to ensure patient safety.

REFERENCES

- CDC’s “Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 Clinical Practice Guideline” and “Clinical Providers’ Supplement”
 - <http://www.cdc.gov/hiv/pdf/PrEPguidelines2014.pdf>
 - <http://www.cdc.gov/hiv/pdf/PrEPProviderSupplement2014.pdf>

RESOURCES

- UCSF HIVE
 - <http://www.hiveonline.org/for-providers>
- San Francisco City Clinic – PrEP Resources for Providers
 - <http://www.sfcityclinic.org/services/prep.asp#Providers>
- UCSF Clinician Consultation Center (PEP expert consultation and resources)
 - <http://nccc.ucsf.edu/clinician-consultation/post-exposure-prophylaxis-pep/>