Providing HIV Pre-Exposure Prophylaxis (PrEP): Protocol\textsuperscript{1} for Edison Clinic

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\textsuperscript{1} Adapted from CDC’s “Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 Clinical Practice Guideline”

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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
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.)
- 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
  - 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

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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
      - 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
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

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**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.

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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 ≥ 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 ≥ 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”

RESOURCES

- UCSF HIVE
  - [http://www.hiveonline.org/for-providers](http://www.hiveonline.org/for-providers)
- San Francisco City Clinic – PrEP Resources for Providers
  - [http://www.sfcityclinic.org/services/prep.asp#Providers](http://www.sfcityclinic.org/services/prep.asp#Providers)
- UCSF Clinician Consultation Center (PEP expert consultation and resources)