PrEP Protocol

This PrEP protocol is adapted from US Public Health Service. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States**: *2017 Update Clinical Practice Guideline***. 2017.

Refer or schedule anyone with any of the following risk factors for a PrEP consult:

- Current injection drug use (IDU)
- Any sex partner(s) of unknown HIV status
- Men who have sex with men (MSM)
- Partner with HIV
- Sexually transmitted infection (STI) in the past 6 months

Referral Process:

- If you do not feel comfortable providing PrEP to your patient, refer to the PrEP Program.
    - Select specialty: PrEP Program.
    - Write the patient's risk factors and reason for referral.
    - Assign to the provider to which the patient is being referred.
    - If the patient is pregnant, trying to become pregnant, or breastfeeding, refer to OB for management.

RISK ASSESSMENTS:

Risk Behavior Assessment for HIV Acquisition through Sexual Contact

These sexual history questions can be found in the HPI sexual history section.

In the past 6 months:

- Have you had sex with men, women, or both?
- How many partners have you had sexual contact with?
- Were any of your partners know to have HIV?
- How many times have you had vaginal or anal receptive intercourse (bottom) with a partner who did not wear a condom?
- How many times did you have insertive anal sex (top) without wearing a condom?
- Have you used methamphetamines (crystal or speed)?

If the patient has a partner with HIV:

- Is the partner on antiretroviral therapy?
- Does the partner have a detectable viral load when last tested?

Risk Assessment for HIV Acquisition through Injection Practices - refer from Behavioral Health

- Have you ever injected drugs not prescribed to you by a clinician?
- When did you last inject drugs that were not prescribed to you?
- In the past 6 months, have you injected by using needles, syringes, or other drug preparation equipment that has already been used by another person?
- In the past 6 months, have you been in a methadone or other medication-based drug treatment program?

Ineligibility Criteria for PrEP

- Truvada® (TDF/FTC) should not be prescribed to a patient with eCrCl of <60 ml/min.*
    - eCrCl can be calculated using the Cockcroft-Gault formula at the link below: https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation
    - *for men with abnormal eCrCL, Descovy® (TAF/FTC) is an option
- Descovy® (TAF/FTC) should not be prescribed to women at risk of vaginal acquisition given an absence of efficacy data to date

- For women at risk of vaginal acquisition of HIV, Truvada is recommended

- A positive 4th generation HIV antigen/antibody test or a detectable quantitative HIV-1 RNA PCR (HIV viral load)
  - HIV 4th generation antigen/antibody test has >99.7% sensitivity and >99.3% specificity for HIV and can identify >80% of acute infections.[1]
  - HIV-1 RNA PCR can detect HIV-1 infection 6-12 days after exposure.[2]
- Signs/symptoms of acute HIV infection in the last 30 days (fever, fatigue, myalgia, rash, headache, sore throat, cervical lymphadenopathy, arthralgia, night sweats, diarrhea)
  - If acute symptoms of HIV are present, test HIV-1/2 antigen/antibodies, 4th Generation with Reflexes (test code:91431, CPT:87389),
    AND
    HIV-1 RNA, Quantitative, Real-Time PCR (CPT:87536, test code: 40085).
  - If the above antigen/antibody are negative and HIV-1 RNA PCR are undetectable, repeat in 1 month, defer PrEP temporarily until repeat testing is available.

INDICATIONS FOR TREATMENT:

Indications for PrEP use by MSM

- Without acute or established HIV infection
  or
- Any male sex partners in past 6 months
  or
- Not in a monogamous partnership with a recently-tested, HIV-negative person
  and at least one of the following:
- Any anal sex without condoms (receptive or insertive) in the past 6 months
- A bacterial STI (syphilis, gonorrhea, or chlamydia) diagnosed or reported in the past 6 months
- Is in an ongoing sexual relationship with a partner with HIV

Indications for PrEP use by Heterosexually Active People

- Without acute or established HIV infection
  or
- Any sex with opposite sex partners in past 6 months
  or
- Not in a monogamous partnership with a recently-tested HIV-negative partner
  and at least one of the following:
  - Has sex with multiple genders
  - Infrequently uses condoms during sex with 1 or more partners of unknown HIV status who are known to be at substantial risk of HIV infection
  - Is in an ongoing sexual relationship with a partner with HIV
  - A bacterial STI (syphilis, gonorrhea, chlamydia) diagnosed or reported in the past 6 months

Indications for PrEP use by Persons Who Inject Drugs

- Without acute or established HIV infection

[1] HIV Infection, Laboratory Testing for Diagnosis and Management. Quest Diagnostics. https://www.questdiagnostics.com/testcenter/testguide.action?dc=TG_HIV_Management&tabview=true. Accessed January 2, 2019.
[2] HIV Infection, Laboratory Testing for Diagnosis and Management. Quest Diagnostics. https://www.questdiagnostics.com/testcenter/testguide.action?dc=TG_HIV_Management&tabview=true. Accessed January 2, 2019.

and

- Any injection of drugs not prescribed by a clinician in the past 6 months
  and at least one of the following:
  - Any sharing of injection or drug preparation equipment in the past 6 months
  - Risk of sexual acquisition
    - Any sex partners in the past 6 months

    or
    - Not in a monogamous partnership with a recently-tested HIV-negative partner

    and at least one of the following:
      - For MSM: any anal sex without condoms (receptive or insertive) in the past 6 months
      - A bacterial STI (syphilis, gonorrhea, chlamydia) diagnosed or reported in the past 6 months
      - For heterosexually active people: Has sex with multiple genders
      - Infrequently uses condoms during sex with one or more partners of unknown HIV status who are known to be at substantial risk of HIV infection
      - Is in an ongoing sexual relationship with an HIV-positive partner

Indications for PrEP use by Individuals with Partner(s) with HIV

- Transmission rate is low if the HIV-positive partners is on antiretroviral therapy with virologic suppression.
- If the partner with HIV is initiating antiretroviral therapy, PrEP may be appropriate during the time that it takes for virologic suppression to be achieved.
- After a partner achieves virologic suppression and undetectable viral load, the extent of decreased risk of HIV transmission with the use of PrEP is unknown.
- Patients should be allowed to continue on PrEP while partner has undetectable viral load if they wish, since blips in viral load can occur, making transmission more likely at those times.

PrEP use in Adolescents (ages 13-17)

- Approved by the FDA for use in adolescents weighing 35 kg or more.
- At this time, PrEP is able to be prescribed in Connecticut without parental consent according to state law. For other states, please refer to local guidelines.
- Adolescents receiving PrEP may require closer follow-up to ensure adherence.

PrEP Use in Preconception, Pregnancy, and Breastfeeding

- Refer to OBGYN for management
- Indicated if the patient has a partner with HIV
  - The partner should be receiving HIV treatment and ideally have undetectable viral load
  - PrEP should be taken for at least 30 days prior to attempts at conception and 30 days after conception.
    - Refer to GYN for education on when chances of conception are highest and only have unprotected intercourse at those times.
  - Other conception options include insemination of women with HIV or insemination with donor sperm or lab-analyzed semen from the man with HIV
- Counsel patient on potential and unknown risks and benefits of PrEP during pregnancy for the fetus and the mother.
  - Truvada® and Descovy® are used in patients with HIV including among those who are pregnant and breastfeeding. To date there are no known adverse effects on fetuses.
- Breastfeeding

- Emtricitabine (FTC) and tenofovir (TDF or TAF) may be present in breastmilk. There are no known adverse effects on babies to date.

Prior to prescribing PrEP

Before prescribing, screen for acute HIV infection with symptoms occurring in the past month. Symptoms include:

- Fever
- Fatigue
- Myalgia
- Skin rash
- Headache
- Sore throat
- Cervical adenopathy
- Arthralgia
- Night sweats
- Diarrhea

If acute symptoms of HIV are present, test HIV-1/2 antigen/antibodies, 4th Generation with Reflexes (test code:91431, CPT:87389)

and

HIV-1 RNA, Quantitative, Real-Time PCR (CPT:87536, test code: 40085)

If the above are negative (or undetectable), repeat in 1 month, defer PrEP temporarily until repeat testing is negative/undetectable.

- HIV-1 RNA PCR can detected infection 6-12 days after exposure[3]
- HIV-1/2 Antigen and Antibodies, 4th Generation with Reflexes can detect HIV within 20 days of exposure[4]

Test the following:

- HIV 4th generation antigen/antibody blood test
  - Negative HIV 4th generation antigen/antibody test documented within 1 week of starting PrEP
  - Must have documentation of result from the lab
  - If test is positive, see below for further testing and confirmation
- Renal function
  - Truvada® should not be prescribed to a patient with eCrCl of <60 ml/min.
    - eCrCl can be calculated using the Cockcroft-Gault formula at the link below: https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation
- Hepatitis B virus (HBV) serology
  - If not immune to HBV, the patient should be vaccinated
  - If HBsAg is positive, refer for treatment by Infectious Disease
    - HBV infection is NOT a contraindication for PrEP, but HBV DNA quantitative assay should be performed every 6 months while on PrEP
    - If a patient has HBV and PrEP is stopped, closely monitor for hepatic damage due to increase HBV replication
- Hepatitis C virus (HCV) testing

[3] HIV Infection, Laboratory Testing for Diagnosis and Management. Quest Diagnostics. https://www.questdiagnostics.com/testcenter/testguide.action?dc=TG_HIV_Management&tabview=true. Accessed January 2, 2019.
[4] HIV Infection, Laboratory Testing for Diagnosis and Management. Quest Diagnostics. https://www.questdiagnostics.com/testcenter/testguide.action?dc=TG_HIV_Management&tabview=true. Accessed January 2, 2019.

- Test Hepatitis C Antibody with Reflex to HCV, RNA, Quantitative Real-Time PCR (CPT:86803, Test code:8472)
  - if positive, PrEP is not contraindicated but patients should be referred for hepatis C treatment
- If there is a known recent exposure, test for hepatitis C RNA
  - Antibodies will develop in 2-6 months following exposure

- Syphilis testing
- Gonorrhea/chlamydia testing - urine test, throat swab, rectal swab if at risk due to sexual activity
- Urine pregnancy test

Monitoring Tests

F/u 1 month after starting

- Confirm HIV-negative status
- Assess for side effects
- Address adherence issues

Every 3 months - must have results prior to refilling medication

- HIV 4th generation antigen/antibody test
- Gonorrhea/chlamydia testing - pharyngeal, rectal, and urine specimens
  - Vaginal and rectal swabs can be obtained by the patient
- Assess side effects, adherence, risk behaviors*
- Counsel on risk reduction strategies
- Provide support for medication adherence
- With adolescent patients, monthly check-in appointments should be scheduled on a patient by patient basis to increase adherence

Every 6 months

- Syphilis testing
- Check renal function

Every 12 months

- Hepatitis C testing if there are ongoing risk factors present such as MSM and IDU
- Evaluate continued need for PrEP

**** If a patient has been off of PrEP for >7 days, retest HIV 4th generation antigen/antibody test***

If a patient was on nonoccupational postexposure prophylaxis (nPEP) and wants to start PrEP:

- Complete risk behavior assessment (refer to risk behavior assessments on page 1)
- Finish 28 days course of nPEP
- HIV 4th generation antibody/antigen test (CPT: 87389, Quest test code: 91431)
- If HIV test is negative and there are no signs/symptoms of acute infection (fever, fatigue, myalgia, rash, headache, sore throat, cervical lymphadenopathy, arthralgia, night sweats, diarrhea), continue the TDF/FTC daily and discontinue the other antiretroviral medication (e.g., dolutegravir or raltegravir). Complete other testing as you would when starting PrEP normally.

If discontinuing PrEP, document the following:

- HIV status
- Reason for discontinuation of treatment
- Recent medication adherence and reported risk behavior

PrEP Protocol

Patient and provider checklists and handouts about PrEP, Truvada® or Descovy®, and signs/symptoms of acute HIV infection are available on the company drive. These should be filled out, scanned, and given to patient before or when PrEP is initiated.

Prescribing PrEP

- Prescribe Truvada® (tenofovir disoproxil fumarate (TDF) 300 mg/emtricitabine 200 mg) or Descovy® (tenofovir alafenamide 25 mg/emtricitabine 200 mg) once daily.
- Do not prescribe more than 90 days of medication at a time.
- The patient should be tested for HIV at their scheduled appointment, but refills of medications should be sent only after a negative result is received.
- The patient must come in for HIV testing prior to receiving a refill of the medication. HIV test should be ordered one week prior to appointment so that result is present when the patient is seen in the office and the medication can be refilled. There must be a documented negative HIV test within 7 days prior to refilling medication.
- It takes 20 days to reach effective concentrations in the blood and cervicovaginal tissue and 7 days to reach effective concentration in rectal tissue.
- Patients should be encouraged to use condoms regardless of PrEP use, although the likelihood of transmission of HIV from a virally-suppressed partner to a seronegative partner is very low[5].

Risk Reduction Counseling

PrEP should be accompanied by a discussion on risk-reducing behaviors. These include:

- Safe sexual practices - condom use, talking to their partners about their HIV status and sexual history
- Referral for clean needles
- Referral to substance use treatment services
- If patient has a partner with unknown HIV status, offer to test the partner or provide information on where they can be tested: www.hivtest.org

Patient Education

- PrEP should be taken daily or it is not as effective
- If they miss a dose, take the missed dose unless it is almost time for the next dose
- They will need to follow up and have blood tests done every 3 months to continue with PrEP
- PrEP does not protect against other STIs
- Patients should still use condoms
- Common side effects
- Risk Reduction Tool https://wwwn.cdc.gov/hivrisk/
- It takes 20 days to reach effective concentrations in the blood and cervicovaginal tissue and 7 days to reach effective concentration in rectal tissue.

Common Side Effects for Truvada® (TDF/FTC) or Descovy® (TAF/FTC):

- Headache
- Nausea
- Flatulence
- There has been some evidence of loss of bone mineral density with tenofovir disoproxil (Truvada®)

[5] Rodger, AJ, Camniano V, Brunn T, et al. Sexual Activity Without Condoms and Risk of HIV Transmission in Serodifferent Couples When the HIV-Positive Partner Is Using Supporessive Antiretroviral Therapy. *JAMA.* 2016;316(2):171. doi: 10.1001/jama.2016.5148

PrEP Protocol

HIV Risk Reduction

- Refer to nurse or to clinical pharmacist for counseling on risk reduction.
    - Condom use - discuss ways to approach this subject with partners
    - Practice ways of asking partners their sexual history and HIV status for safer sexual practices
        - https://www.cdc.gov/condomeffectiveness/docs/male-condom-use-508.pdf
        - https://www.cdc.gov/condomeffectiveness/dental-dam-use.html
    - Regular (at least once every 3-6 months) bacterial STI screening and testing if at risk
    - Discontinuing IDU- referral to MAT program
    - Education on sharing injection drug preparation and administration equipment