TRUVADA for a Pre-exposure Prophylaxis (PrEP) Indication

Training Guide for Healthcare Providers
About TRUVADA for a PrEP indication to reduce the risk of sexually acquired HIV-1 infection in high-risk adults

INDICATION
TRUVADA (emtricitabine/tenofovir disoproxil fumarate) is indicated in combination with safer sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults at high risk.* This indication is based on clinical trials in men who have sex with men (MSM) at high risk for HIV-1 infection and in heterosexual serodiscordant couples.

PRESCRIBING CONSIDERATIONS: When prescribing TRUVADA for pre-exposure prophylaxis:
• Only prescribe TRUVADA as part of a comprehensive prevention strategy because TRUVADA is not always effective in preventing the acquisition of HIV-1
• Counsel all uninfected individuals to strictly adhere to their TRUVADA daily dosing schedule because the effectiveness of TRUVADA in reducing the risk of acquiring HIV-1 is strongly correlated with adherence and measurable drug levels
• Confirm a negative HIV-1 test immediately prior to initiating TRUVADA for a PrEP indication. If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposures are suspected, delay starting PrEP for at least 1 month and reconfirm HIV-1 status or use a test approved by the FDA as an aid in the diagnosis of HIV-1 infection, including acute or primary HIV-1 infection
• Screen for HIV-1 infection at least once every 3 months while taking TRUVADA for PrEP
• Do not prescribe TRUVADA for a PrEP indication if signs or symptoms of acute HIV infection are present unless negative infection status is confirmed

*Factors that may help to identify individuals at high risk include individuals having partner(s) known to be HIV-1 infected or engaging in sexual activity within a high prevalence area or social network and one or more of the following: inconsistent or no condom use, diagnosis of sexually transmitted infections, exchange of sex for commodities (such as money, food, shelter, or drugs), use of illicit drugs or alcohol dependence, incarceration, or partner(s) of unknown HIV-1 status with any of the factors listed above.

BOXED WARNINGS: Use of TRUVADA for a PrEP Indication
• TRUVADA used for a PrEP indication must only be prescribed to individuals confirmed to be HIV-1 negative immediately prior to initial use and periodically (at least every 3 months) during use. Drug-resistant HIV-1 variants have been identified with the use of TRUVADA for a PrEP indication following undetected acute HIV-1 infection. Do not initiate TRUVADA for a PrEP indication if signs or symptoms of acute HIV infection are present unless negative infection status is confirmed
• Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including VIREAD, a component of TRUVADA
• TRUVADA is not approved for the treatment of chronic hepatitis B virus (HBV) infection. Severe acute exacerbations of hepatitis B have been reported in patients coinfected with HIV-1 and HBV who have discontinued TRUVADA. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who are infected with HBV and discontinue TRUVADA. If appropriate, initiation of anti-hepatitis B therapy may be warranted
Why Use TRUVADA for a PrEP Indication?

By inhibiting HIV-1 from replicating as it enters the body, TRUVADA for a PrEP indication works to prevent the virus from establishing permanent infection. However, TRUVADA should not be seen as the first line of defense against HIV-1. Because TRUVADA is not always effective in preventing the acquisition of HIV-1, TRUVADA for a PrEP indication must be used in combination with a comprehensive prevention strategy that includes safer sex practices, such as regular and correct condom use, regular HIV-1 testing for themselves (and their sexual partners), and other proven HIV-1 prevention methods to safely and effectively reduce the risk of acquiring HIV-1.

- TRUVADA for a PrEP indication must only be prescribed to uninfected individuals at high risk who are confirmed to be HIV-1 negative
- Uninfected individuals who are prescribed TRUVADA for a PrEP indication should not miss any doses. Missing doses raises the risk of acquiring HIV-1

TRUVADA is also indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection. TRUVADA should never be used alone in an individual infected with HIV-1 because of the increased risk of resistance. Therefore, it is critical to confirm negative HIV-1 status. Confirm a negative HIV-1 test immediately prior to initiating TRUVADA for a PrEP indication. If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposures are suspected, delay starting PrEP for at least 1 month and reconfirm HIV-1 status or use a test approved by the FDA as an aid in the diagnosis of HIV-1 infection, including acute or primary HIV-1 infection. Screen for HIV-1 infection at least once every 3 months while taking TRUVADA for PrEP.

Key Findings of the TRUVADA for a PrEP Indication Trials

The iPrEx Trial

- In one clinical trial of TRUVADA for a PrEP indication, TRUVADA was shown to reduce the risk of HIV-1 acquisition by 42% for high risk men who have sex with men who also received comprehensive prevention services, including monthly HIV-1 testing, condom provision, counseling, and management of other sexually transmitted infections
- In a post hoc case control study of plasma and intracellular drug levels in about 10% of clinical trial subjects, risk reduction appeared to be the greatest in subjects with detectable intracellular tenofovir. Efficacy was therefore strongly correlated with adherence
- Because of the intensive risk reduction counseling provided as part of the trial, self-reported risk behavior among the subjects in this clinical trial declined overall during the trial, both in terms of decreases in the number of sexual partners and increases in condom use

The Partners PrEP Trial

- In another clinical trial of TRUVADA for a PrEP indication in serodiscordant couples, TRUVADA was shown to reduce HIV-1 acquisition by 75% for the uninfected individuals exposed to the virus through heterosexual sex
- In a post hoc case control study of plasma drug levels in about 10% of clinical trial subjects, risk reduction appeared to be the greatest in subjects with detectable plasma tenofovir. Efficacy was therefore strongly correlated with adherence
TRUVADA Safety Profile

IMPORTANT SAFETY INFORMATION

Contraindication: TRUVADA for a PrEP indication is contraindicated in individuals with positive or unknown HIV-1 status.

Warnings and Precautions Relating to the Use of TRUVADA for a PrEP Indication

• Comprehensive management to reduce the risk of acquiring HIV-1: TRUVADA for a PrEP indication should only be used as part of a comprehensive prevention strategy that includes other prevention measures, such as safer sex practices, because TRUVADA is not always effective in preventing the acquisition of HIV-1

  – Counsel uninfected individuals at high risk about safer sex practices, including:
    • Using condoms consistently and correctly
    • Knowing their HIV-1 status and that of their partner(s)
    • Being tested for other sexually transmitted infections
    • Informing individuals about the importance of reducing sexually risky behaviors and supporting their efforts to do so

  – Use TRUVADA to reduce the risk of acquiring HIV-1 only in individuals confirmed to be HIV-1 negative. HIV resistance substitutions may emerge with individuals with undetected HIV-1 infection who are taking only TRUVADA because TRUVADA alone does not constitute a complete treatment regimen for HIV-1 infection. Therefore:
    • Confirm a negative HIV-1 test immediately prior to initiating TRUVADA for a PrEP indication. If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposures are suspected, delay starting PrEP for at least 1 month and reconfirm HIV-1 status or use a test approved by the FDA as an aid in the diagnosis of HIV-1 infection, including acute or primary HIV-1 infection
    • Screen for HIV-1 infection at least once every 3 months while taking TRUVADA for PrEP

  – Counsel all uninfected individuals to strictly adhere to their TRUVADA daily dosing schedule. The effectiveness of TRUVADA in reducing the risk of acquiring HIV-1 is strongly correlated with adherence and measurable drug levels

• New onset or worsening renal impairment: Can include acute renal failure and Fanconi syndrome. Assess creatinine clearance (CrCl) before prescribing TRUVADA. Monitor CrCl and serum phosphorus in individuals at risk for renal impairment. Avoid administering TRUVADA with concurrent or recent use of nephrotoxic drugs

  – Do not prescribe TRUVADA for a PrEP indication for uninfected individuals with a creatinine clearance below 60 mL/min. If a decrease in CrCl is observed in uninfected individuals while using TRUVADA for PrEP, evaluate potential causes and re-assess potential risks and benefits of continued use

• HBV infection: It is recommended that all individuals be tested for the presence of chronic hepatitis B virus (HBV) before initiating TRUVADA

  – HBV-uninfected individuals should be offered vaccination

• Decreases in bone mineral density (BMD): Consider assessment of BMD in individuals with a history of pathologic fracture or other risk factors for osteoporosis or bone loss

• Redistribution/accumulation of body fat: Observed in patients receiving antiretroviral therapy

• Immune reconstitution syndrome: May necessitate further evaluation and treatment in HIV-1–infected patients

  – Evaluate for signs or symptoms of acute HIV-1 infection prior to and while prescribing TRUVADA for a PrEP indication. If symptoms consistent with acute HIV-1 infection develop following a potential exposure event, PrEP should be discontinued until negative infection status is confirmed using a test approved by the FDA as an aid in the diagnosis of HIV-1, including acute or primary HIV-1 infection
Important Safety Information About the Use of TRUVADA for a PrEP Indication in Specific Populations

• **Pregnancy:** There are no adequate and well-controlled trials in pregnant women. TRUVADA should be used during pregnancy only if clearly needed. If an uninfected individual becomes pregnant while taking TRUVADA for a PrEP indication, careful consideration should be given to whether use of TRUVADA should be continued, taking into account the potential increased risk of HIV-1 infection during pregnancy
  
  — A pregnancy registry is available. Enroll women taking TRUVADA for a PrEP indication by calling 1-800-258-4263

• **Nursing mothers:** Women infected with HIV-1 or taking TRUVADA for a PrEP indication should be instructed not to breast-feed. The components of TRUVADA (emtricitabine and tenofovir disoproxil fumarate) are excreted in breast milk, and it is not known if these can harm the infant

• **Pediatrics:** The TRUVADA for a PrEP indication is based on trials in adults

Reminder about the use of TRUVADA for a PrEP indication: It is important to confirm and regularly reconfirm negative HIV-1 status before and while the individual is taking TRUVADA for a PrEP indication.

• Confirm a negative HIV-1 test immediately prior to initiating TRUVADA for a PrEP indication. If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposures are suspected, delay starting PrEP for at least 1 month and reconfirm HIV-1 status or use a test approved by the FDA as an aid in the diagnosis of HIV-1 infection, including acute or primary HIV-1 infection

• Screen for HIV-1 infection at least once every 3 months while taking TRUVADA for PrEP

• It is important to be alert to the signs of potential acute HIV-1 infection when prescribing TRUVADA for a PrEP indication. These include fever, headache, fatigue, arthralgia, vomiting, myalgia, diarrhea, pharyngitis, rash, night sweats, and cervical and inguinal adenopathy

• If symptoms consistent with acute HIV-1 infection develop following a potential exposure event, PrEP should be discontinued until negative infection status is confirmed using a test approved by the FDA as an aid in the diagnosis of HIV-1, including acute or primary HIV-1 infection

• HIV-1 resistance mutations may emerge in individuals with undetected HIV-1 infection who are taking TRUVADA for a PrEP indication

Use the Checklist for Prescribers and the Agreement Form to help manage and counsel individuals about the correct and safe use of TRUVADA for a PrEP indication.

Important Safety Information

Drug Interactions

• **Coadministration with other products**
  
  — Do not use TRUVADA with drugs containing emtricitabine or tenofovir disoproxil fumarate, or with drugs containing lamivudine. Do not administer in combination with HEPSERA® (adefovir dipivoxil)
  
  — Caution should be exercised when co-administering TRUVADA with didanosine, atazanavir, or lopinavir/ritonavir due to the potential for toxicities

For further details about TRUVADA drug interactions, please see Full Prescribing Information for TRUVADA in back pocket.
Common Adverse Events

• In HIV-1–uninfected individuals in PrEP trials, adverse reactions that were reported by more than 2% of TRUVADA subjects and more frequently than by placebo subjects were headache, abdominal pain, and weight decreased

• The most common adverse events (incidence ≥10%) reported by HIV-1–infected subjects in clinical trials (in combination with efavirenz) are diarrhea, nausea, fatigue, headache, dizziness, depression, insomnia, abnormal dreams, and rash

For more information about TRUVADA and its indication for PrEP, please see the Full Prescribing Information, including Boxed WARNINGS and Medication Guide. For more information about the REMS program for TRUVADA for a PrEP indication, please log on to www.TRUVADAprepregs.com. You may also obtain additional information and educational materials about the use of TRUVADA for a PrEP indication at 1-800-445-3235.

Post-Training Review Questions

1. TRUVADA for a PrEP indication should be used only:
   a. As part of a comprehensive HIV-1 prevention strategy that includes other preventive measures since TRUVADA is not always effective in preventing the acquisition of HIV-1
   b. In individuals who have been counseled to strictly adhere to their TRUVADA daily dosing schedule since the effectiveness of TRUVADA in reducing the risk of acquiring HIV-1 is strongly correlated with adherence and measurable drug levels
   c. In individuals who have a confirmed negative HIV-1 test prior to initiating and routinely while taking TRUVADA for a PrEP indication
   d. All of the above

2. Which of the following statements is false?
   a. TRUVADA should be used for a PrEP indication only in individuals confirmed to be HIV-1 negative
   b. TRUVADA has been found to be safe and effective for pre-exposure prophylaxis to reduce the risk of acquiring HIV-1 through injection drug use
   c. Women taking TRUVADA for a PrEP indication should not breast-feed their babies
   d. TRUVADA for a PrEP indication is not always effective in preventing HIV-1

3. Which of the following items are not included on the Checklist for Prescribers for initiating TRUVADA for a PrEP indication?
   a. Perform HBV screening test
   b. Perform testing for TB
   c. Confirm negative HIV-1 status of the individual
   d. Confirm creatinine clearance is ≥60 mL/min

For more information about TRUVADA and its indication for PrEP, please see the Full Prescribing Information, including Boxed WARNINGS and Medication Guide. For more information about the REMS program for TRUVADA for a PrEP indication, please log on to www.TRUVADAprepregs.com. You may also obtain additional information and educational materials about the use of TRUVADA for a PrEP indication at 1-800-445-3235.
4. Hepatic function should be monitored closely in:
   a. HBV-infected individuals who discontinue TRUVADA
   b. All people taking TRUVADA
   c. All people who discontinue TRUVADA
   d. None of the above

5. In clinical trials evaluating TRUVADA for a PrEP indication, which of the following adverse reactions was not common?
   a. Abdominal pain
   b. Headache
   c. Dizziness
   d. Decreased weight

6. TRUVADA for a PrEP indication is indicated only for:
   a. Men who are at high risk for sexually acquired HIV-1 infection
   b. Adults who are at high risk of acquiring HIV-1 infection by any means
   c. Adults who are at high risk of acquiring HIV-1 infection through injection drug use
   d. Adults who are at high risk for sexually acquired HIV-1 infection

7. The Agreement Form for Initiating TRUVADA for PrEP of Sexually Acquired HIV-1 Infection provides which of the following information:
   a. A list of activities that put individuals at risk for sexually acquired HIV-1
   b. A confirmation that the prescriber has discussed the risks and benefits of using TRUVADA for a PrEP indication with the uninfected individual
   c. A signature from the individual asserting that the prescriber has explained the risks and benefits of taking TRUVADA for a PrEP indication, including the need for adherence and a comprehensive prevention strategy, which includes safer sex practices
   d. All of the above

Answer key: 1-d; 2-b; 3-b; 4-a; 5-c; 6-d; 7-d
If you would like additional educational materials about TRUVADA for a PrEP indication, please select which ones you want and how many you would like us to send to you.

Quantity:

☐ Important Safety Information for Uninfected Individuals ☐ 10 ☐ 25 ☐ 50
☐ Important Safety Information for Healthcare Providers ☐ 10 ☐ 25 ☐ 50
☐ TRUVADA Medication Guide ☐ 10 ☐ 25 ☐ 50
☐ Safety Information Fact Sheet ☐ 10 ☐ 25 ☐ 50
☐ Checklist for Prescribers ☐ 10 ☐ 25 ☐ 50
☐ Agreement Form ☐ 10 ☐ 25 ☐ 50

Your full name and degree: ______________________________________
Street address: _________________________________________________
City: __________________________  State: _______  ZIP: ____________

Your practice or clinic name: _____________________________________
Your specialty: _________________________________________________
Telephone: ________________  E-mail: ___________________________

Terms and Conditions
Gilead Sciences, Inc., and its authorized agents agree only to use the above information for purposes of fulfilling your request for additional materials regarding TRUVADA for a PrEP indication and will not transfer your information to any other party unless required to do so for the sole purpose of completing your request.