TRUVADA® for a Pre-exposure Prophylaxis (PrEP) Indication

Healthcare Provider Training
Pre-exposure Prophylaxis (PrEP) 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 infection 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.
Factors to Help Identify Individuals at High Risk

- Has a partner known to be HIV-1 infected, or
- Engages 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
  - Partner(s) of unknown HIV-1 status with any of the factors listed above
When Prescribing TRUVADA for a PrEP Indication, Healthcare Providers MUST:

- Prescribe TRUVADA as part of a comprehensive prevention strategy because TRUVADA is not always effective in preventing the acquisition of HIV-1 infection.
- Counsel all uninfected individuals to strictly adhere to the recommended daily TRUVADA dosing schedule because the effectiveness of TRUVADA in reducing the risk of acquiring HIV-1 infection 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 signs or symptoms consistent with acute viral infection are present or recent (<1 month) exposures are suspected,
  - delay starting PrEP for at least one 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.
- While using TRUVADA for a PrEP indication, HIV-1 screening tests should be repeated at least every 3 months.
  - 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 infection, including acute or primary HIV-1 infection.
TRUVADA used for a PrEP indication must only be prescribed to individuals confirmed to be HIV negative immediately prior to initiating 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.
BOXED WARNING, cont.

- 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 infected with HBV who have discontinued TRUVADA. Therefore, 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 infection.
- Because TRUVADA is not always effective in preventing the acquisition of HIV-1 infection, 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 testing for themselves (and their sexual partners), and other proven HIV prevention methods to safely and effectively reduce the risk of acquiring HIV-1 infection.
  - 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 may increase the risk of acquiring HIV-1 infection.
Key Findings of the TRUVADA for a PrEP Indication Studies: 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 study, self-reported risk behavior among the subjects in this clinical study declined overall during the study, both in terms of decreases in the number of self-reported sexual partners and increases in condom use.
Key Findings of the TRUVADA for a PrEP Indication Studies: The Partners PrEP Trial

- In another clinical study of TRUVADA for a PrEP indication, TRUVADA was shown to reduce HIV-1 acquisition by 75% in uninfected individuals in stable heterosexual serodiscordant relationships who also received comprehensive prevention services, including monthly HIV testing, evaluation of adherence, assessment of sexual behavior, and safety evaluations.

- In a post-hoc case control study of plasma drug levels in about 10% of study subjects, risk reduction appeared to be the greatest in subjects with detectable plasma tenofovir. Efficacy was therefore strongly correlated with adherence. Risk reduction increased further in subjects with detectable plasma tenofovir.
Important Safety Information: Comprehensive Management to Reduce the Risk of Acquiring HIV-1

- Prescribe TRUVADA for PrEP only as part of a comprehensive prevention strategy that includes other prevention measures, such as safer sex practices, because TRUVADA for a PrEP indication is not always effective in preventing the acquisition of HIV-1 infection
  - Counsel uninfected individuals about safer sex practices that include consistent and correct use of condoms, knowledge of their HIV-1 status and that of their partner(s), and regular testing for other sexually transmitted infections that can facilitate HIV-1 transmission (such as syphilis and gonorrhea)
  - Inform uninfected individuals about and support their efforts in reducing sexual risk behavior
Important Safety Information: Comprehensive Management to Reduce the Risk of Acquiring HIV-1 Infection

- Prescribe TRUVADA to reduce the risk of acquiring HIV-1 only in individuals confirmed to be HIV negative
  - HIV-1 resistance substitutions may emerge in individuals with undetected HIV-1 infection who are taking only TRUVADA, because TRUVADA alone does not constitute a complete regimen for HIV-1 treatment; therefore, care should be taken to minimize drug exposure in HIV-infected individuals
- Many HIV-1 tests, such as rapid tests, detect anti-HIV antibodies and may not identify HIV-1 during the acute stage of infection. Prior to initiating TRUVADA for a PrEP indication, evaluate seronegative individuals for current or recent signs and symptoms consistent with acute viral infections and ask about potential exposure events that may have occurred within the last month
Important Safety Information: Comprehensive Management to Reduce the Risk of Acquiring HIV-1 Infection

- Confirm a negative HIV-1 test immediately prior to initiating TRUVADA for a PrEP indication. If clinical signs or symptoms consistent with acute viral infection are present or recent (<1 month) exposures are suspected,
  - delay starting PrEP for at least one 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

- While using TRUVADA for a PrEP indication, HIV-1 screening tests should be repeated at least every 3 months.
  - 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 infection, including acute or primary HIV-1 infection
Important Safety Information: Comprehensive Management to Reduce the Risk of Acquiring HIV-1 Infection

- Counsel uninfected individuals to strictly adhere to the recommended daily TRUVADA dosing schedule. The effectiveness of TRUVADA for a PrEP indication in reducing the risk of acquiring HIV-1 infection is strongly correlated with adherence and measurable drug levels.
Important Safety Information: Additional Warnings and Precautions

New Onset or Worsening Renal Impairment
- Can include acute renal failure and Fanconi syndrome
- Assess estimated creatinine clearance (CrCl) before prescribing TRUVADA and periodically during therapy with TRUVADA
- In patients at risk of renal dysfunction, monitor estimated CrCl, serum phosphorus, urine glucose and urine protein before prescribing TRUVADA and periodically while TRUVADA is being used
Important Safety Information: Additional Warnings and Precautions

New Onset or Worsening Renal Impairment

- Avoid administering TRUVADA with concurrent or recent use of nephrotoxic drugs. Cases of acute renal failure, some requiring hospitalization and renal replacement therapy have been reported after initiation of high dose or multiple NSAIDs in patients with risk factors for renal dysfunction; consider alternatives to NSAIDs in these patients.

- Do not prescribe TRUVADA for a PrEP indication in HIV-1 uninfected individuals with an estimated CrCl below 60 mL/min
  - If a decrease in estimated CrCl is observed in uninfected individuals while using TRUVADA for a PrEP indication, evaluate potential causes and re-assess potential risks and benefits of continued use.

Reference ID: 3526740
Important Safety Information: Additional Warnings and Precautions

Bone effects

- Decreases in bone mineral density (BMD) and mineralization defects, including osteomalacia, have been seen in patients treated with tenofovir disoproxil fumarate. Consider assessment of BMD in individuals with a history of pathologic fracture or other risk factors for osteoporosis or bone loss.

- Persistent or worsening bone pain, pain in extremities, fractures and/or muscular pain or weakness may be manifestations of proximal renal tubulopathy and should prompt an evaluation of renal function in at-risk patients.
Important Safety Information: Additional Warnings and Precautions

Redistribution/accumulation of body fat
- Observed in patients receiving antiretroviral therapy for treatment of HIV-1 infection

HBV Infection
- It is recommended that all individuals be tested for the presence of chronic HBV before initiating TRUVADA
- HBV-uninfected individuals should be offered vaccination

Coadministration with other products
- Do not use TRUVADA with drugs containing emtricitabine or tenofovir disoproxil fumarate, with drugs containing lamivudine, or with adefovir dipivoxil
Important Safety Information: 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 in 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 the use of TRUVADA should be continued, taking into account the potential increased risk of HIV infection during pregnancy*
- A pregnancy registry is available. Enroll pregnant women taking TRUVADA for a PrEP indication by calling 1-800-258-4263

Important Safety Information: Use of TRUVADA for a PrEP Indication in Specific Populations

Nursing Mothers
- The components of TRUVADA are excreted in breast milk. Because the risks to the infant are not known, mothers taking TRUVADA for a PrEP indication should be instructed not to breastfeed. If an uninfected individual acquires HIV-1 infection, it is recommended that she not breastfeed to avoid risking postnatal transmission of HIV-1 infection.

Pediatrics
- TRUVADA for a PrEP indication is based on trials in adults.
Important Safety Information: Confirming and Regularly Reconfirming Negative HIV-1 Status

- TRUVADA should be used to reduce the risk of acquiring HIV-1 infection only in individuals confirmed to be HIV-1 negative
  - A negative HIV-1 status should be confirmed before prescribing TRUVADA for a PrEP indication
  - Individuals should be regularly tested (at least every 3 months) while taking TRUVADA for a PrEP indication to reconfirm that they are HIV-1 negative
  - 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: Confirming and Regularly Reconfirming Negative HIV-1 Status

• Potential for Resistance in Undetected Acute HIV-1 Infection
  – 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
  – HIV-1 resistance mutations may emerge in individuals with undetected HIV-1 infection who are taking TRUVADA for a PrEP indication
    • Although TRUVADA is active against HIV-1, TRUVADA alone does not constitute a complete treatment regimen for HIV-1 infection
    • HIV-1–infected patients taking TRUVADA must take it with other antiretroviral agents to fully suppress virus replication and avoid the development of resistance
Important Safety Information: Drug Interactions and Common Adverse Events

Drug Interactions
- Coadministration with drug that reduce renal function or compete for active tubular secretion may increase concentrations of tenofovir
  - For further details about TRUVADA drug interactions, please see Prescribing Information for TRUVADA

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 decreased weight.
Additional Educational Materials

- **Agreement Form for Initiating TRUVADA for PrEP of Sexually Acquired HIV-1 Infection**
  - Designed for prescribers to use with uninfected individuals to facilitate discussion of appropriate use of TRUVADA for a PrEP indication
  - Form covers safety risks associated with use of TRUVADA for a PrEP indication, the importance of adherence to the recommended daily dosing regimen, regular assessment of HIV-1 test results, and screening for sexually transmitted infections

- **Checklist for Prescribers: Initiation of TRUVADA for PrEP**
  - Checklist of key components for prescribers to consider before starting an uninfected individual on TRUVADA for a PrEP indication
  - Checklist items include confirming a negative HIV-1 test result, screening for signs or symptoms of acute HIV-1 infection, counseling on safety risks and importance of adherence, and other components to ensure a comprehensive prevention strategy

- **Copies are available from [www.TRUVADApreeprems.com](http://www.TRUVADApreeprems.com) or by filling out business reply card at the back of the Training Guide for Healthcare Providers booklet**
Additional Educational Materials

- Additional educational materials can be reviewed and downloaded at [www.TRUVADApreprems.com](http://www.TRUVADApreprems.com)
- Please confirm completion of training by going to [www.TRUVADApreprems.com](http://www.TRUVADApreprems.com) or by filling out business reply card at the back of the Training Guide for Healthcare Providers booklet
- Gilead is conducting a survey to fulfill an FDA Risk Evaluation and Mitigation Strategy (REMS) requirement to assess prescribers’ knowledge regarding important safety information associated with the use of TRUVADA for a PrEP indication. To participate, please go to [www.TRUVADApreprems.com](http://www.TRUVADApreprems.com) or fill out the BRC at the back of the Training Guide for Healthcare Providers booklet