Important Safety Information About TRUVADA for a Pre-exposure Prophylaxis (PrEP) Indication

For Healthcare Providers
About TRUVADA for a PrEP Indication

INDICATION AND PRESCRIBING CONSIDERATIONS
TRUVADA, a combination of emtricitabine and 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.

The following factors may help to identify individuals at high risk:

• Has partner(s) 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 a sexually transmitted infection (STI)
  – Exchange of sex for commodities (such as money, food, shelter, or drugs)
  – Use of illicit drugs, alcohol dependence
  – Incarceration
  – Partner(s) of unknown HIV-1 status with any of the factors listed above

When prescribing TRUVADA for a PrEP indication:

• Only 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 their TRUVADA daily 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 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 uninfected individuals for HIV-1 infection at least once every 3 months while taking TRUVADA for a PrEP indication
• Do not prescribe TRUVADA for a PrEP indication if signs or symptoms of acute HIV-1 infection are present unless negative infection status is confirmed

Potential for Resistance in Undetected Acute HIV-1 Infection
It is important to be alert to the signs or symptoms of potential acute HIV-1 infection when prescribing TRUVADA for a PrEP indication, including:

• Fever, headache, fatigue, arthralgia, vomiting, myalgia, diarrhea, pharyngitis, rash, night sweats, and adenopathy (cervical and inguinal)

It is recommended that negative HIV-1 status be reconfirmed on a regular basis (at least every 3 months) using HIV-1 screening tests while uninfected individuals are taking TRUVADA for a PrEP indication.
TRUVADA Safety Profile

BOXED WARNING: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS, POST-TREATMENT ACUTE EXACERBATION OF HEPATITIS B, AND RISK OF DRUG RESISTANCE WITH USE OF TRUVADA FOR A PrEP INDICATION IN UNDIAGNOSED EARLY HIV-1 INFECTION

• TRUVADA used for a PrEP indication must only be prescribed to individuals confirmed to be HIV 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-1 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.

Important Safety Information About TRUVADA for a PrEP Indication

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

Warnings and Precautions
• Comprehensive management to reduce the risk of acquiring HIV-1 infection.

TRUVADA for a PrEP indication should be used only 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 infection.

  – 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 regularly tested for other sexually transmitted infections that can facilitate HIV-1 transmission (eg, syphilis and gonorrhea)

  – Inform uninfected individuals at high risk about and support their efforts to reduce sexual risk behavior.

  – Use TRUVADA to reduce the risk of acquiring HIV-1 infection only in individuals confirmed to be HIV-1 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 treatment regimen for HIV-1 infection.
• Confirm a negative HIV-1 test immediately prior to initiating TRUVADA for a PrEP indication. 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 or symptoms consistent with acute viral infections and ask about potential exposure events that may have occurred within the last month. If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposures are suspected, delay starting TRUVADA for a PrEP indication 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 a PrEP indication.

• If symptoms consistent with acute HIV-1 infection develop following a potential exposure event, TRUVADA for a PrEP indication 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.

• Evaluate for signs or symptoms of acute HIV-1 infection prior to prescribing and during treatment with TRUVADA for a PrEP indication.

  – Counsel all uninfected individuals to strictly adhere to a daily dosing schedule for TRUVADA. 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 estimated creatinine clearance (CrCl) before prescribing and during treatment 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. 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.

  – For pre-exposure prophylaxis: Do not prescribe TRUVADA for 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 reassess potential risks and benefits of continued use.

• **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.

• **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.

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

• **Coadministration with other products:** Do not use TRUVADA with drugs containing emtricitabine or tenofovir disoproxil fumarate, with drugs containing lamivudine, or with adeovir dipivoxil.
Important Safety Information

Common Adverse Reactions With TRUVADA

- 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.

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:** The components of TRUVADA (emtricitabine/tenofovir disoproxil fumarate) 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:** The TRUVADA for a PrEP indication is based on trials in adults.

TRUVADA Drug Interactions

For further details about TRUVADA drug interactions, please see the full Prescribing Information for TRUVADA in back pocket.

Use the Checklist for Prescribers: Initiation of TRUVADA for Pre-exposure Prophylaxis (PrEP) and the Agreement Form for Initiating TRUVADA for Pre-exposure Prophylaxis (PrEP) to help manage and counsel individuals about the safe use of TRUVADA for a PrEP indication.

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