IMPORTANT DRUG WARNING

Subject: FDA-Required Risk Evaluation Mitigation Strategy (REMS) for TRUVADA®
[TRUVADA for a pre-exposure prophylaxis (PrEP) indication]

A negative HIV-1 test must be confirmed immediately before starting
TRUVADA for a PrEP indication and reconfirmed during treatment. Drug-resistant HIV-1 variants have been identified with the use of TRUVADA for a
PrEP indication following undetected HIV-1 infection.

Dear Healthcare Provider:

Gilead Sciences, Inc., would like to inform you of the FDA-approved REMS for
TRUVADA (a fixed-dose combination of emtricitabine 200 mg and tenofovir disoproxil
fumarate 300 mg) for a PrEP indication in combination with safer sex practices to
reduce the risk of sexually acquired HIV-1 infection in adults at high risk. TRUVADA for
a PrEP 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 FDA has determined that a REMS is necessary to ensure that the benefits of
TRUVADA for a PrEP indication outweigh its risks.

The goals of the REMS for TRUVADA for a PrEP indication are to inform and educate
prescribers and uninfected individuals at high risk for acquiring HIV-1 infection about:

- The importance of strict adherence to the recommended dosing regimen

- The importance of regular monitoring of HIV-1 serostatus to avoid continuing to take
TRUVADA for a PrEP indication, if seroconversion has occurred, to reduce the risk
of development of resistant HIV-1 variants

- The fact that TRUVADA for a PrEP indication must be considered as only a part of a
comprehensive prevention strategy in order to reduce the risk of HIV-1 infection and
that other preventive measures should also be used.

Before initiating TRUVADA for a PrEP indication

You MUST confirm a negative HIV-1 status immediately before prescribing TRUVADA
for a PrEP indication in an uninfected individual. Drug-resistant HIV-1 variants have
been identified with use of TRUVADA for a PrEP indication following undetected HIV-1 infection.

Do NOT prescribe TRUVADA for a PrEP indication to patients with HIV-1 infection or to individuals with signs or symptoms consistent with acute HIV-1 infection, such as fever, headache, fatigue, arthralgia, vomiting, myalgia, diarrhea, pharyngitis, rash, night sweats, and adenopathy (cervical and inguinal).

**Prescriber Action**

You should review and discuss the content of the Agreement Form for Initiating TRUVADA for Pre-exposure Prophylaxis with an HIV-negative person considering or taking TRUVADA for a PrEP indication and refer to the Checklist for Prescribers: Initiation of TRUVADA for Pre-exposure Prophylaxis (PrEP) regarding the management of an uninfected individual taking TRUVADA for a PrEP indication. (Access Agreement Form and Checklist via www.TRUVADApreams.com)

The most important information you should know about prescribing TRUVADA for a PrEP indication to reduce the risk of acquiring HIV-1 infection is:

- TRUVADA for a PrEP indication should only be used as part of a comprehensive prevention strategy including consistent and correct use of condoms and risk reduction counseling

- All uninfected individuals at high risk for acquiring HIV-1 infection should only take TRUVADA for a PrEP indication after HIV-1 negative status is confirmed, to reduce the risk of development of resistant HIV-1 variants

- All uninfected individuals at high risk must strictly adhere to the recommended TRUVADA for a PrEP indication daily oral regimen

**Management of Uninfected Individuals**

Uninfected individuals at high risk should:

- Be counseled about safer sex practices, including 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

- Be tested to confirm that they are HIV-1 negative immediately before starting TRUVADA for a PrEP indication

- Be tested for acute HIV-1 infection and checked for any signs or symptoms consistent with acute HIV-1 infection, such as fever, headache, fatigue, arthralgia,
vomiting, myalgia, diarrhea, pharyngitis, rash, night sweats, and adenopathy (cervical and inguinal)

- Be screened at least every 3 months for HIV-1 status as determined by their prescriber to reconfirm that they are HIV-1-negative while taking TRUVADA for a PrEP indication to reduce the risk of acquiring HIV-1 infection

- Have their creatinine clearance (CrCl) estimated prior to initiating and as clinically appropriate during therapy with TRUVADA. Do NOT use TRUVADA for a PrEP indication if the estimated CrCl is <60 mL/min. In patients at risk for renal dysfunction, assess estimated CrCl, serum phosphorus, urine glucose, and urine protein before initiation of TRUVADA, and periodically during TRUVADA therapy. If a decrease in estimated CrCl is observed in uninfected individuals while using TRUVADA for a PrEP indication, the prescriber should evaluate potential causes and reassess potential risks and benefits of continued use

- Be tested for the presence of hepatitis B virus (HBV) before starting on TRUVADA for a PrEP indication. Severe acute exacerbations of hepatitis B have been reported in individuals who are co-infected with HBV and HIV-1 and have discontinued TRUVADA. Uninfected individuals taking TRUVADA for a PrEP indication who are infected with HBV need close medical follow-up for several months to monitor for exacerbations of hepatitis B in the event TRUVADA is discontinued. HBV-uninfected individuals should be offered vaccination as appropriate

- Be informed about the risk of lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, which have been reported. TRUVADA should be suspended in any patient who develops clinical symptoms suggestive of lactic acidosis or pronounced hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked transaminase elevations)

- Be informed that TRUVADA has only been evaluated in a limited number of women during pregnancy and postpartum. Available human and animal data suggest that TRUVADA does not increase the risk of major birth defects overall compared to the background rate. There are, however, no adequate and well-controlled trials in pregnant women. Because the studies in humans cannot rule out the possibility of harm, 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.
REMS Website (www.TRUVADAPreprems.com)

The REMS website provides access to the following:

- Specific information regarding the risks of TRUVADA for a PrEP indication
- Training and educational materials for prescribers and uninfected individuals considering or taking TRUVADA for a PrEP indication, including the Agreement Form for Initiating TRUVADA for Pre-exposure Prophylaxis (PrEP) and Checklist for Prescribers: Initiation of TRUVADA for Pre-exposure Prophylaxis (PrEP)
- A mechanism to report completion of review of the training material
- A link to participate in the Knowledge, Attitude, and Behavior (KAB) REMS survey regarding important safety information associated with the use of TRUVADA for a PrEP indication

Reporting Adverse Events

To report any adverse events, suspected to be associated with the use of TRUVADA for a PrEP indication, contact:

- Gilead Sciences, Inc., at 1-800-445-3235 and/or
- FDA’s MedWatch reporting system by phone (1-800-FDA-1088), by facsimile (1-800-FDA-0178), or online (https://www.accessdata.fda.gov/scripts/medwatch/)

This letter is not intended as a comprehensive description of the risks associated with the use of TRUVADA for a PrEP indication. Please read the enclosed Prescribing Information, including the BOXED WARNING, and the Medication Guide for more information.

Sincerely,

Hans Reiser, MD
Senior Vice President, Medical Affairs