

Initial REMS Approval: 07/16/2012
Most Recent Approval: 03/2016

NDA 021752

TRUVADA® (emtricitabine/tenofovir disoproxil fumarate)

Nucleoside/Nucleotide Analog Human Immunodeficiency Virus-1

Reverse Transcriptase Inhibitors

**Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404**

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOALS

The goals of the REMS for TRUVADA for a Pre-Exposure Prophylaxis (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 part of a comprehensive prevention strategy to reduce the risk of HIV-1 infection and that other preventive measures should also be used

II. REMS ELEMENTS

A. Elements to Assure Safe Use

1. Gilead Sciences, Inc. (Gilead) will ensure that training and education through the TRUVADA for a PrEP Indication Healthcare Provider Education Program is available to healthcare providers (HCPs) who prescribe TRUVADA for a PrEP indication.
 - a. Gilead will ensure that training and education materials will be available for completion by HCPs who prescribe TRUVADA for a PrEP indication via the TRUVADA for a PrEP Indication Healthcare Provider Education Program on the REMS website (www.TRUVADAprEPREMS.com) or via hard copy available upon request. This information will remain on the REMS website for a period of 3 years from initial approval.
 - b. Gilead will ensure that prescribers can report that they have completed the TRUVADA for a PrEP Indication Healthcare Provider Education Program online or via a postage paid business reply card.
 - c. Gilead will maintain a secure database with a list of HCPs who have completed the prescribers training.
 - d. Gilead's training efforts will target the following HCPs who are likely to prescribe TRUVADA for a PrEP indication:
 - Primary care physicians, including internal medicine, family practice, and general medicine physicians
 - Infectious Diseases specialists
 - Obstetrician-gynecologists
 - Addiction specialists
 - e. In order to facilitate prescriber training and education, Gilead will disseminate information about the potential and known safety risks with TRUVADA for a PrEP indication to select professional organizations representing the HCPs likely to prescribe TRUVADA for a PrEP indication as described in d. above.
 - i. The Safety Information Fact Sheet for Prescribers about TRUVADA for a Pre-exposure Prophylaxis (PrEP) Indication will be available for distribution on the TRUVADA for a PrEP Indication REMS website or via hard copy for select professional organizations to disseminate to HCPs bi-annually, for 3 years.

- ii. The Safety Information Fact Sheet for Prescribers About TRUVADA for a Pre-exposure Prophylaxis (PrEP) Indication will include:
 - 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 part of a comprehensive prevention strategy to reduce the risk of HIV-1 infection and that other preventive measures should also be used
- iii. Within 60 days of product approval or at the time of product launch, whichever is sooner, and again at 6, 12, and 24 months, Gilead will send the Safety Information Fact Sheet to the following professional organizations:
 - HIV Medicine Association/Infectious Diseases Society of America
 - American Academy of HIV Medicine
 - Association of Nurses in AIDS Care
 - National Medical Association
 - American Academy of Family Physicians
 - American Society of Addiction Medicine
 - American College of Obstetricians and Gynecologists
 - National Association of Community Health Centers
 - National Association of City and County Health Officials
 - American College of Preventive Medicine
 - National Association of Public Hospitals
 - American Pharmacists Association

The Safety Information Fact Sheet for Prescribers about TRUVADA for a Pre-exposure Prophylaxis (PrEP) Indication will be provided to MedWatch at the same time it is provided to these professional organizations.

The Safety Information Fact Sheet for Prescribers about TRUVADA for a Pre-exposure Prophylaxis (PrEP) Indication is part of the REMS and is appended.

- f. In order to facilitate prescriber training and education, Gilead will disseminate printed safety information (above) about the use of TRUVADA for a PrEP indication to target HCPs through select professional scientific journals:
- i. Journal information pieces will be published quarterly as printed information in the following professional society journals for 3 years following initial approval of the REMS:
- Journal of the American Medical Association
 - Journal of the Academy of Family Physicians
 - Obstetricians and Gynecologists
 - Clinical Infectious Diseases
 - New England Journal of Medicine

The journal information piece is part of the REMS and is appended

- g. Gilead will ensure that, as part of training and education, the following materials are available to HCPs:
- i.. **Dear Healthcare Provider (DHCP) letter** will include the potential and known risks associated with the use of TRUVADA for a PrEP indication and explain how to access the relevant training and education materials provided by Gilead. The letter will be sent to HCPs who are likely to prescribe TRUVADA for a PrEP indication, as described in d. above. The letter will be sent within 60 days of product approval or at the time of product launch, whichever is sooner, and again after 6, 12 and 24 months. The Prescribing Information will also be available with the DHCP letter. The letter will be available on the TRUVADA for a PrEP Indication REMS website on the date of the first mailing.

Gilead will distribute the DHCP letter to the targeted HCPs via electronic mail, mail, or facsimile.

- ii. **Important Safety Information about TRUVADA for a PrEP Indication for Healthcare Providers and Important Safety Information about TRUVADA to Reduce the Risk of Getting Human Immunodeficiency Virus-1 (HIV-1) Infection** will include both information directed to prescribers for education, as well as safety risk information for prescribers to use to educate uninfected individuals considering or taking TRUVADA for a PrEP indication.
- iii. Prescribers will have access to the **Agreement Form for Initiating TRUVADA for Pre-Exposure Prophylaxis (PrEP)** to be discussed with an uninfected individual taking TRUVADA for a PrEP indication. The Agreement Form will be for use at each visit to facilitate discussion of and promote understanding about the safety risks associated with the use of TRUVADA for a PrEP indication, the importance of adherence to the

recommended daily dosing regimen, monitoring HIV-1 test results, and screening for sexually transmitted infections. The prescriber and the uninfected individual will sign the Agreement Form and the form will be placed in the individual's medical record.

- iv. Prescribers will have access to a **Checklist for Prescribers: Initiation of TRUVADA for Pre-exposure Prophylaxis (PrEP)** as a reminder for the management of an uninfected individual considering or taking TRUVADA for a PrEP indication, recommendations for screening laboratory test results including a negative HIV-1 test result, sexually transmitted infections, signs and symptoms of acute HIV-1 infection and hepatitis B, vaccination, as needed, to ensure a comprehensive prevention strategy for prescribing TRUVADA for a PrEP indication in an uninfected individual.
- v. The posting on the REMS Website for TRUVADA for a PrEP Indication and/or a mailing will include the TRUVADA for a PrEP Indication Healthcare Provider Training and Education Program which will consist of the following materials to support the training and educational process:
 - 1. Prescribing Information
 - 2. Dear Healthcare Provider Letter
 - 3. Training Guide for Healthcare Providers
 - 4. Healthcare Provider Education Slide Deck
 - 5. Important Safety Information about TRUVADA for a PrEP Indication for Healthcare Providers
 - 6. Important Safety Information about TRUVADA to Reduce the Risk of Getting Human Immunodeficiency Virus-1 (HIV-1) Infection
 - 7. Agreement Form for Initiating TRUVADA for Pre-Exposure Prophylaxis (PrEP)
 - 8. Checklist for Prescribers: Initiation of TRUVADA for Pre-exposure Prophylaxis (PrEP) to manage an uninfected individual considering or taking TRUVADA for a PrEP indication
 - 9. Safety Information Fact Sheet for Prescribers about TRUVADA for a Pre-exposure Prophylaxis (PrEP) Indication

These materials are part of the REMS and are appended.

- h. Gilead will ensure that all materials listed in or appended to the TRUVADA for a PrEP Indication program will be available through the TRUVADA REMS program website, www.truvadapreprems.com, within 30 days of the most recent REMS

modification approval. This information will remain on the website for a period of 3 years from product approval.

B. Timetable for Submission of Assessments

Gilead Sciences, Inc. will submit REMS Assessments to FDA annually from the initial date of the approval (07/16/12) of the REMS for the first year and every 18 months, thereafter. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Gilead Sciences, Inc. will submit each assessment so that it will be received by the FDA on or before the due date.

Safety Information Fact Sheet for Prescribers

About TRUVADA® for a 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.

BOXED WARNING SPECIFIC FOR USING 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 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.

Key Safety Information to Communicate Regarding the Use of TRUVADA for a PrEP Indication:

1. Risk of Development of Drug-Resistant HIV-1 Variants in Undiagnosed HIV-1–Infected Individuals

- HIV-1 variants with resistance have emerged in individuals taking TRUVADA for a PrEP indication with undetected acute HIV-1 infection
 - You must 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 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, 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 for a PrEP indication is contraindicated in individuals with unknown or HIV-1–positive status**
- Do not prescribe TRUVADA for a PrEP indication if signs or symptoms of acute HIV infection are present unless negative infection status is confirmed

– HIV-1–infected patients must take TRUVADA in combination with other antiretroviral agents to fully suppress virus replication and avoid the development of resistance

2. Only Use TRUVADA for a PrEP Indication as Part of a Comprehensive Prevention Strategy

- TRUVADA for a PrEP indication does not replace other HIV-1 infection prevention measures, including safer sex practices and correct and consistent condom use
- Clinical trials included comprehensive prevention counseling, screening for and treatment of other sexually transmitted infections, and strong emphasis regarding consistent use of condoms and other safer sex practices

3. The Importance of Strict Adherence to the Recommended Dosing Regimen

- 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
- All uninfected individuals at high risk taking TRUVADA for a PrEP indication must be counseled to strictly adhere to the recommended daily dosing schedule to reduce the risk of acquiring HIV-1 infection

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.TRUVADAprerepms.com. You may also obtain additional information and educational materials about the use of TRUVADA for a PrEP indication at 1-800-445-3235.



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Truvada®
emtricitabine-tenofovir disoproxil fumarate

Important Information for Prescribers About TRUVADA[®] for a 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.

BOXED WARNING SPECIFIC FOR USING 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 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.

Key Safety Information to Communicate Regarding the Use of TRUVADA for a PrEP Indication:

1. Risk of Development of Drug-Resistant HIV-1 Variants in Undiagnosed HIV-1–Infected Individuals

- HIV-1 variants with resistance have emerged in individuals taking TRUVADA for a PrEP indication with undetected acute HIV-1 infection
- You must 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 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 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 infection, including acute or primary HIV-1 infection
 - **TRUVADA for a PrEP indication is contraindicated in individuals with unknown or HIV-1–positive status**
- Do not prescribe TRUVADA for a PrEP indication if signs or symptoms of acute HIV infection are present unless negative infection status is confirmed
 - HIV-1–infected patients must take TRUVADA in combination with other antiretroviral agents to fully suppress virus replication and avoid the development of resistance

2. Only Use TRUVADA for a PrEP Indication as Part of a Comprehensive Prevention Strategy

- TRUVADA for a PrEP indication does not replace other HIV-1 infection prevention measures, including safer sex practices and correct and consistent condom use
- Clinical trials included comprehensive prevention counseling, screening for and treatment of other sexually transmitted infections, and strong emphasis regarding consistent use of condoms and other safer sex practices

3. The Importance of Strict Adherence to the Recommended Dosing Regimen

- 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
- All uninfected individuals at high risk taking TRUVADA for a PrEP indication must be counseled to strictly adhere to the recommended daily dosing schedule to reduce the risk of acquiring HIV-1 infection

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.TRUVADAprereps.com. You may also obtain additional information and educational materials about the use of TRUVADA for a PrEP indication at 1-800-445-3235.



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Truvada[®]
emtricitabine-tenofovir disoproxil fumarate

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.TRUVADAprereps.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.TRUVADAprereps.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,

William Guyer, PharmD
Senior Vice President, Medical Affairs

REMS-TVD-0002 03/16

Truvada®

²⁰⁰mg emtricitabine · tenofovir disoproxil fumarate ³⁰⁰mg

**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 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 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 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 WARNING:

- **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-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 infected with 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**

Truvada[®]

200 emtricitabine - tenofovir disoproxil fumarate 300

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-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 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 raises the risk of acquiring HIV-1 infection

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 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 infection 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 infection 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[®]

200 emtricitabine - tenofovir disoproxil fumarate 300

TRUVADA Safety Profile

IMPORTANT SAFETY INFORMATION

Contraindications:

- 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 regularly tested for other sexually transmitted infections that can facilitate HIV-1 transmission (eg, syphilis and gonorrhea)
 - 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. 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 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
- Evaluate for signs or symptoms of acute HIV-1 infection prior to prescribing and during treatment with 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
 - 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 estimated creatinine clearance (CrCl) before prescribing and periodically 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

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– Do not prescribe TRUVADA for a PrEP indication 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 PrEP, 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, tenofovir disoproxil fumarate, or tenofovir alafenamide, with drugs containing lamivudine, or with adefovir dipivoxil

Important Safety Information

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

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:** The components of TRUVADA (emtricitabine and 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
- **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

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- 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

Drug Interactions

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 correct and safe use of TRUVADA for a PrEP indication.

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

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.TRUVADAprereps.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:

- 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 infection
- 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 infection is strongly correlated with adherence and measurable drug levels
- In individuals who have a confirmed negative HIV-1 test prior to initiating and routinely while taking TRUVADA for a PrEP indication
- All of the above

2. Which of the following statements is false?

- TRUVADA should be used for a PrEP indication only in individuals confirmed to be HIV-1 negative
- TRUVADA has been found to be safe and effective for pre-exposure prophylaxis to reduce the risk of acquiring HIV-1 infection through injection drug use
- Women taking TRUVADA for a PrEP indication should not breastfeed their babies
- TRUVADA for a PrEP indication is not always effective in preventing HIV-1 infection

3. Which of the following items are not included on the Checklist for Prescribers: Initiation of TRUVADA for Pre-exposure Prophylaxis (PrEP)?

- Perform HBV screening test
- Perform testing for TB
- Confirm negative HIV-1 status of the individual
- Confirm creatinine clearance is ≥ 60 mL/min

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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 Pre-exposure Prophylaxis (PrEP) provides which of the following information:

- a. A list of activities that put individuals at risk for sexually acquired HIV-1 infection
- 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

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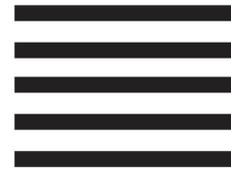
Help uninfected individuals learn more about TRUVADA for a pre-exposure prophylaxis (PrEP) indication



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Reference ID: 3900321

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 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 is strongly correlated with adherence and detectable blood 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 PrEP - 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, including acute or primary HIV-1 infection

BOXED WARNING

- 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-1 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, in combination with other antiretrovirals
- 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 coinfecting with HIV-1 and 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
- 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 testing for themselves (and their sexual partners), and other proven HIV 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 may increase the risk of acquiring HIV

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 trial 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 is not always effective in preventing the acquisition of HIV-1
 - 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

- 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 (e.g., fever, fatigue, myalgia, skin rash, etc.) and ask about potential exposure events (e.g., unprotected, or condom broke during sex with an HIV-1 infected partner) that may have occurred within the last month

Important Safety Information: Comprehensive Management to Reduce the Risk of Acquiring HIV-1

- 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 PrEP, 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, including acute or primary HIV-1 infection

Important Safety Information: Comprehensive Management to Reduce the Risk of Acquiring HIV-1

- Counsel uninfected individuals to strictly adhere to the recommended daily TRUVADA dosing schedule. The effectiveness of TRUVADA in reducing the risk of acquiring HIV-1 is strongly correlated with adherence as demonstrated by measurable drug levels in a subgroup of clinical trials subjects

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
- In individuals at risk of renal impairment, assess 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 use 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 PrEP, evaluate potential causes and re-assess potential risks and benefits of continued use

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 DF. 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

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

Coadministration with other products

- Do not use TRUVADA with drugs containing emtricitabine, tenofovir disoproxil fumarate, or tenofovir alafenamide, 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

*Gray RH, et al. Lancet 2005;366(9492):1182-1188

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 PrEP 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

Pediatrics

- TRUVADA for a PrEP indication is based on trials in adults

Important Safety Information: Confirming and Regularly Reconfirming Negative HIV Status

- TRUVADA should be used to reduce the risk of acquiring HIV-1 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 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 of TRUVADA with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of tenofovir.
- For further details about TRUVADA drug interactions, please see full 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 weight decreased.

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 infection, counseling on safety risks and importance of adherence, and other components to ensure a comprehensive prevention strategy
- Copies available from www.TRUVADAprereps.com or by filling out business reply card at back of the Training Guide for Healthcare Providers booklet

Additional Educational Materials

- Additional educational materials can be reviewed and downloaded at www.TRUVADAprereps.com
- Please confirm completion of training by going to www.TRUVADAprereps.com or by filling out business reply card at 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.TRUVADAprereps.com or fill out the BRC at the back of the Training Guide for Healthcare Providers booklet

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²⁰⁰mg emtricitabine · tenofovir disoproxil fumarate ³⁰⁰mg

**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.

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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 coinfecting 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

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- 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, tenofovir disoproxil fumarate, or tenofovir alafenamide, with drugs containing lamivudine, or with adefovir dipivoxil

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 250 emtricitabine • tenofovir disoproxil fumarate 300

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.TRUVADAprereps.com. You may also obtain additional information and educational materials about the use of TRUVADA for a PrEP indication at 1-800-445-3235.

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Reference: TRUVADA [package insert]. Foster City, CA: Gilead Sciences, Inc; 2016.



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Important Safety Information About TRUVADA to Reduce the Risk of Getting Human Immunodeficiency Virus–1 (HIV-1) Infection

This booklet is for adults taking TRUVADA to reduce the risk of getting HIV-1 infection.

If you are taking TRUVADA to treat HIV-1, please see the Medication Guide for other important information.

TRUVADA to Reduce the Risk of Getting HIV-1 Infection

TRUVADA (emtricitabine/tenofovir disoproxil fumarate) is a prescription medicine to reduce the chance of getting HIV-1 infection in adults when used with safer sex practices. HIV is the virus that causes AIDS (Acquired Immune Deficiency Syndrome).

TRUVADA, to reduce the risk of getting HIV-1 infection, is meant for adults who are:

- HIV negative, and
- At high risk for getting HIV-1 infection through sex

TRUVADA only works to reduce the risk of getting HIV-1 infection as part of a complete prevention strategy that includes safer sex practices and regular testing for HIV-1.

- TRUVADA works better to reduce the risk of getting HIV-1 infection when the medicines are in your bloodstream *before* you are exposed to HIV-1
- You need to take TRUVADA every day, not just when you think you have been exposed
- Just taking TRUVADA alone may not keep you from getting HIV-1 infection

You must be HIV negative to start TRUVADA. You must get tested to make sure that you do not already have HIV-1 infection. Do not take TRUVADA to reduce the risk of getting HIV-1 infection unless you are confirmed to be HIV negative.

The most important information you should know about TRUVADA

TRUVADA can cause serious side effects, including:

- 1. Too much lactic acid in your blood (lactic acidosis).** Your body normally makes lactic acid, but too much lactic acid can be a serious medical emergency. It can be treated, but it can also lead to death.

Call your healthcare provider right away if you get these symptoms:

- Weakness or being more tired than usual
- Unusual muscle pain
- Being short of breath or fast breathing
- Nausea, vomiting, and stomach-area pain
- Cold or blue hands and feet
- Feeling dizzy or lightheaded
- Fast or abnormal heartbeats

You may be more likely to get lactic acidosis if you are a woman, are very overweight (obese), or have been taking TRUVADA for a long time.

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2. Severe liver problems. Severe liver problems can happen in people who take TRUVADA. In some cases, these liver problems can lead to death. Your liver may become large and tender. You may develop fat in your liver when you take TRUVADA.

Call your doctor or nurse right away if you get these symptoms:

- Your skin or the white part of your eyes turns yellow
- Dark “tea-colored” urine
- Light-colored stools
- Loss of appetite for several days or longer
- Nausea
- Stomach-area pain

You may be more likely to get severe liver problems if you are a woman, are very overweight (obese), or have been taking TRUVADA for a long time.

3. If you also have hepatitis B virus (HBV) infection and take TRUVADA, your hepatitis B may become worse if you stop taking TRUVADA.

- Do not stop taking TRUVADA without first talking with your healthcare provider
- If your healthcare provider stops TRUVADA, your healthcare provider will need to watch you closely for several months to check your hepatitis B infection, or give you a medication to treat hepatitis B

Tell your healthcare provider about any new or unusual symptoms you have after you stop taking TRUVADA.

Before taking TRUVADA to reduce your risk of getting HIV-1 infection

- **You must be HIV negative to start TRUVADA.** You must get tested to make sure that you do not already have HIV-1 infection
- Many HIV-1 tests can miss HIV-1 infection in a person who has recently become infected. If you have flu-like symptoms, you could have recently become infected with HIV-1. Tell your healthcare provider if you had a flu-like illness within the last month before starting TRUVADA or at any time while taking TRUVADA. Symptoms of new HIV-1 infection include:
 - Tiredness
 - Fever
 - Joint or muscle aches
 - Headache
 - Sore throat
 - Vomiting or diarrhea
 - Rash
 - Night sweats
 - Enlarged lymph nodes in the neck or groin

While you are taking TRUVADA to reduce your risk of getting HIV-1 infection:

- **Just taking TRUVADA alone may not keep you from getting HIV-1 infection**

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- **You must continue using safer sex practices** while you are taking TRUVADA to reduce your risk of getting HIV-1 infection
- **You must stay HIV-1 negative to keep taking TRUVADA to reduce your risk of infection**
 - Know your HIV-1 status and the HIV-1 status of your partners
 - Get tested for HIV-1 at least every 3 months or when your healthcare provider tells you
 - Get tested for other sexually transmitted infections, such as syphilis and gonorrhea. These infections make it easier for HIV-1 to infect you
 - If you think you were exposed to HIV-1, tell your healthcare provider right away. Your healthcare provider may want to do more tests to be sure you are still HIV negative
 - Get information and support to help reduce risky sexual behavior
 - Have fewer sex partners
 - Do not miss any doses of TRUVADA. Missing doses may increase your risk of getting HIV infection
- If you do become HIV positive, you need more medicine than TRUVADA alone to treat HIV-1 infection. TRUVADA by itself is not a complete treatment for HIV-1 infection
 - If you have HIV-1 and take only TRUVADA, over time your HIV-1 infection may become harder to treat

See the section **“Things you should avoid while taking TRUVADA”** and talk with your healthcare provider for more information about how to prevent HIV-1 infection.

Things you should avoid while taking TRUVADA

There are things you should avoid while taking TRUVADA that can increase your risk of getting infected with HIV-1. While taking TRUVADA:

- Do NOT have any kind of sex without protection. Always practice safer sex. Use latex or non-latex condoms, except lambskin, to reduce contact with semen, vaginal fluids, or blood
- Do NOT share personal items that can have blood or body fluids on them, such as toothbrushes and razor blades
- Do NOT share or reuse needles or other injection equipment

Ask your healthcare provider if you have any questions about how to prevent getting infected with HIV-1

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Do not take TRUVADA to reduce the risk of getting HIV-1 infection if...

TRUVADA can only help reduce your risk of getting HIV-1 **before** you are infected. **Do not take TRUVADA to reduce the risk of getting HIV-1 infection if:**

- **You already have HIV-1 infection.** If you are HIV positive, you need to take other medicines with TRUVADA to treat HIV-1. TRUVADA by itself is not a complete treatment for HIV-1 infection
- **You do not know your HIV-1 infection status.** You may already be HIV positive. You need to take over HIV-1 medicines with TRUVADA to treat HIV-1 infection

Things to tell your healthcare provider before taking TRUVADA

Tell your healthcare provider if you:

- **Have liver problems, including hepatitis B virus infection**
- **Have kidney problems or receive kidney dialysis treatment**
- **Have bone problems**
- **Have any other medical conditions**
- **Are pregnant or plan to become pregnant.** It is not known if TRUVADA can harm your unborn child

If you are a female who is taking TRUVADA to reduce the risk of getting HIV-1 infection and you become pregnant while taking TRUVADA, talk with your healthcare provider to decide if you should keep taking TRUVADA.

Pregnancy Registry: A pregnancy registry collects information about your health and the health of your baby. There is a pregnancy registry for women who take medicines to treat or prevent HIV-1 during pregnancy. For more information about the registry and how it works, talk with your healthcare provider.

- **Are breastfeeding or plan to breastfeed**
 - If you become HIV-1 positive while taking TRUVADA, do not breastfeed because the virus can pass to your baby through the breast milk
 - Do not breastfeed if you take TRUVADA. TRUVADA can pass to your baby in your breast milk
 - Talk with your healthcare provider about the best way to feed your baby

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Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Do not take TRUVADA if you also take any of the medicines listed below:

- Medicines which also contain emtricitabine or tenofovir disoproxil fumarate (ATRIPLA®, COMPLERA®, EMTRIVA, GENVOYA®, ODEFSEY®, STRIBILD®, or VIREAD). These medicines contain one or more of the same active ingredients as TRUVADA.
- Medicines which contain tenofovir alafenamide (GENVOYA or ODEFSEY)
- Medicines which contain lamivudine (Combivir, Dutrebis, Eпивir, Eпивir-HBV, Epzicom, Triumeq, or Trizivir)
- Adefovir (HEPSERA®)

TRUVADA may interact with other medicines. Especially tell your healthcare provider if you take:

- Didanosine (Videx EC)
- Atazanavir (Reyataz)
- Darunavir (Prezista)
- Lopinavir with ritonavir (Kaletra)
- Ledipasvir with sofosbuvir (Harvoni®)

Your doctor may need to check you more often or change your dose if you take any of these medicines and TRUVADA.

Know the medicines you take. Keep a list of them to show your healthcare provider or pharmacist when you get a new medicine.

How to take TRUVADA

- Take TRUVADA exactly as prescribed
- Take TRUVADA by mouth, with or without food
- TRUVADA is usually taken 1 time each day. Take TRUVADA at the same time each day to keep TRUVADA blood levels constant
- Do not miss any doses of TRUVADA. Missing a dose lowers the amount of medicine in your blood
- If you miss a dose of TRUVADA, take it as soon as you remember that day. Do not take more than 1 dose of TRUVADA in a day. Do not take 2 doses at the same time to make up for a missed dose. Call your healthcare provider or pharmacist if you are not sure what to do
- Do not change your dose or stop taking TRUVADA without first talking with your healthcare provider. Stay under a healthcare provider's care when taking TRUVADA
- Refill your TRUVADA prescription before you run out of medicine
- If you take too much TRUVADA, call your healthcare provider or go to the nearest hospital emergency room right away
- If you take TRUVADA to reduce your risk of getting HIV-1 infection:
- You must also use other methods to reduce your risk of getting infected with HIV-1. See the section “**Things you should avoid while taking TRUVADA**” in this booklet
- **Take TRUVADA every day**, not just when you think you have been exposed to HIV-1

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Possible side effects of TRUVADA

TRUVADA may cause serious side effects, including:

- See “The most important information you should know about TRUVADA”
- **New or worse kidney problems**, including kidney failure. If you have had kidney problems in the past or take medicines that can cause kidney problems, your healthcare provider may do blood tests to check your kidneys before you start and while you are taking TRUVADA. Your healthcare provider may tell you to stop taking it if you have kidney problems
- **Bone problems** can happen in some people who take TRUVADA. Bone problems include bone pain, or softening or thinning of bones, which may lead to fractures. Your healthcare provider may need to do tests to check your bones
- **Changes in body fat** can happen in people who take HIV medicines. The exact cause and long-term health effects of these problems are not known. The changes may include increased amount of fat in the upper back and neck (“buffalo hump”), breast, and around the middle of your body (trunk), and loss of fat from the legs, arms, and face

Common side effects of TRUVADA

Common side effects in people who take TRUVADA to reduce the risk of getting HIV-1 infection include: stomach-area (abdomen) pain, headache, and decreased weight.

Tell your healthcare provider if you have any side effect that bothers you or does not go away.

These are not all of the possible side effects of TRUVADA. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may also report side effects to FDA at 1-800-FDA-1088.

How to store TRUVADA

- Store TRUVADA at room temperature between 68°F to 77°F (20°C to 25°C)
- Keep TRUVADA in its original container and keep the container tightly closed
- Do not use TRUVADA if seal over bottle opening is broken or missing

Keep TRUVADA and all other medicines out of reach of children.

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Notes

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You can find this booklet and other important information about TRUVADA to reduce the risk of getting HIV-1 infection at www.TRUVADAprerequisites.com or call 1-800-445-3235.



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Reference ID: 3900321

Agreement Form

for Initiating TRUVADA[®] for Pre-exposure Prophylaxis (PrEP)

Individual Label

Instructions: Review form with an HIV-negative person who is about to start or is taking TRUVADA for a PrEP indication at each visit. File form in the person's medical record.

TRUVADA 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. 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 sexually transmitted infections
 - Exchange of sex for commodities (such as money, shelter, food, or drugs)
 - Use of illicit drugs, alcohol dependence
 - Incarceration
 - Partner(s) of unknown HIV-1 status with any of the factors listed above

Healthcare Provider Agreement

By signing below, I signify my understanding of the risks and benefits of TRUVADA for a PrEP indication and my obligation as a prescriber to educate the HIV-negative person about these risks, counsel the person on risk reduction, monitor the person appropriately, and report adverse events. Specifically, I attest to having done the following:

- Confirmed the negative HIV-1 status of this person prior to starting TRUVADA for a PrEP indication
- Read the Prescribing Information, including the BOXED WARNING
- Discussed with the HIV-negative person the known safety risks with use of TRUVADA for a PrEP indication
- Reviewed the importance of adherence with a comprehensive prevention strategy, including practicing safer sex
- Discussed the importance of regular HIV-1 testing (at least every 3 months) while taking TRUVADA for a PrEP indication
- Reviewed the TRUVADA Medication Guide with the HIV-negative person at high risk prior to prescribing TRUVADA for a PrEP indication
- Completed the items on the Checklist for Prescribers: Initiation of TRUVADA for Pre-exposure Prophylaxis (PrEP)

Healthcare Provider's
Signature

Date

HIV-Negative Person Agreement

By signing below, I acknowledge that I have talked with my healthcare provider about the risks and benefits of TRUVADA to reduce the risk of getting HIV-1 infection, and I understand them clearly. Specifically, I attest to the following:

- My healthcare provider talked with me about the importance of follow-up HIV-1 testing, and I agree to have repeat HIV-1 screening tests (at least every 3 months) as scheduled by my healthcare provider
- My healthcare provider talked with me about the safety risks involved with using TRUVADA to reduce the risk of getting HIV-1 infection
- My healthcare provider talked with me about a complete prevention strategy and always practicing safer sex by using condoms correctly
- I will talk with my healthcare provider if I have any questions
- I have read the TRUVADA Medication Guide

HIV-Negative Person's
Signature

Date

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Checklist for Prescribers:

Individual Label

Initiation of TRUVADA® for Pre-exposure Prophylaxis (PrEP)

Instructions: Complete checklist at each visit and file in individual's medical record.

I have completed the following prior to prescribing TRUVADA for a pre-exposure prophylaxis (PrEP) indication for the individual who is about to start or is taking TRUVADA for a PrEP indication:

Lab Tests/Evaluation

- Completed high risk evaluation of uninfected individual
- Confirmed 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) exposure is 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. (Note: TRUVADA for a PrEP indication is contraindicated in individuals with unknown HIV-1 status or who are HIV-1 positive)
- Performed HBV screening test
- Confirmed estimated creatinine clearance (CrCl) >60 mL/min prior to initiation and periodically during treatment. In patients at risk for renal dysfunction, assess estimated CrCl, serum phosphorus, urine glucose, and urine protein before initiation of TRUVADA and periodically while TRUVADA is being used. 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
- Confirmed that the uninfected individual at high risk is not taking other HIV-1 medications or HBV medications
- Evaluated risk/benefit for women who may be pregnant or may want to become pregnant

Counseling/Follow-up

- Discussed known safety risks with use of TRUVADA for a PrEP indication
- Counseled on the importance of scheduled follow-up every 2 to 3 months, including regular HIV-1 screening tests (at least every 3 months), while taking TRUVADA for a PrEP indication to reconfirm HIV-1–negative status
- Discussed the importance of discontinuing TRUVADA for a PrEP indication if seroconversion has occurred, to reduce the development of resistant HIV-1 variants
- Counseled on the importance of adherence to daily dosing schedule
- Counseled that TRUVADA for a PrEP indication should be used only as part of a comprehensive prevention strategy
- Educated on practicing safer sex consistently and using condoms correctly
- Discussed the importance of the individual knowing their HIV-1 status and, if possible, that of their partner(s)
- Discussed the importance of and performed screening for sexually transmitted infections (STIs), such as syphilis and gonorrhea, that can facilitate HIV-1 transmission
- Offered HBV vaccination as appropriate
- Provided education on where information about TRUVADA for a PrEP indication can be accessed
- Discussed potential adverse reactions
- Reviewed the TRUVADA Medication Guide with the uninfected individual at high risk

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> TruvadaPrEPremis.com

This document contains copy for the creation of the REMS for TRUVADA for a PrEP Indication HCP Web site.

Revised: March 2016

TruvadaPrEPremis.com Global Items

Area on page	Description and copy
Global Header/Utilities	<p>REMS Information <i>[Links to home page]</i></p> <p>Prescribing Information and Medication Guide <i>[Links to http://www.truvadapreprems.com/pdf/fpi.pdf]</i></p> <p>Important Safety Information including BOXED WARNING <i>[Links to 1.3, Important Safety Information]</i></p>
Global Top Navigation	<p>0.0 TRUVADA for PrEP logo <i>[Links to 0.0 www.TruvadaPrEPremis.com]</i></p> <p>1.0 Prophylaxis therapy <i>[Links to 1.1]</i></p> <p style="padding-left: 20px;">1.1 TRUVADA for a PrEP Indication <i>[Links to 1.1]</i></p> <p style="padding-left: 20px;">1.2 Comprehensive Management <i>[Links to 1.2]</i></p> <p style="padding-left: 20px;">1.3 Important Safety Information <i>[Links to 1.3]</i></p> <p>2.0 Starting Individuals <i>[Links to 2.1]</i></p> <p style="padding-left: 20px;">2.1 Checklist for Prescribers <i>[Links to 2.1]</i></p> <p style="padding-left: 20px;">2.2 Agreement Form <i>[Links to 2.2]</i></p> <p>3.0 Support <i>[Links to 3.1]</i></p> <p style="padding-left: 20px;">3.1 REMS Materials <i>[Links to 3.1]</i></p> <p style="padding-left: 20px;">3.2 Post-Training Review Questions <i>[Links to 3.2]</i></p>

Area on page	Description and copy
Global Footer	<p data-bbox="462 224 734 252">Site Map <i>[Links to 5.0]</i></p> <p data-bbox="462 317 1446 478">The information on this site is intended for audiences 18 years of age or older in the United States only. The content on this site may not apply to non-US audiences as regulatory control, legal requirements and/or medical practices may vary in other countries. Read the full site disclaimer at www.gilead.com/terms_of_use.</p> <div data-bbox="462 562 711 632">  <b data-bbox="532 575 711 611">GILEAD </div> <p data-bbox="462 684 1382 779">TRUVADA, the TRUVADA Logo, GILEAD, the GILEAD Logo, and GSI, are trademarks of Gilead Sciences, Inc., or its related companies. All other marks referenced herein are the property of their respective owners.</p> <p data-bbox="462 825 1300 848">© 2016 Gilead Sciences, Inc. All rights reserved. REMS-TVD-0001 03/16</p>

Global Right Rail Callouts

Area on page	Description and copy
Header over all RR callouts	REMS Center
Right rail callout	<p>Materials</p> <p>Download important materials for healthcare providers and uninfected individuals about TRUVADA for a PrEP indication</p> <p><i>[Links to 4.1]</i></p>
Right rail callout	<p>Post-Training Review Questions</p> <p>Assess your knowledge of TRUVADA for a PrEP indication by answering a series of review questions</p> <p><i>[Links to question 1 of review questions]</i></p>

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[new brand box]	<p>[H1] TRUVADA for a Pre-exposure Prophylaxis (PrEP) Indication</p> <p>[Copy] This is a Risk Evaluation and Mitigation Strategy (REMS) Web site. TRUVADA for a PrEP indication—in combination with safer sex practices—can help reduce the risk of sexually acquired HIV-1 infection as part of a comprehensive HIV-1 prevention strategy in adults at high risk. TRUVADA for a PrEP indication does not replace existing prophylaxis strategies. Review factors that can help healthcare providers identify individuals at high risk for sexually acquired HIV-1 infection and important prescribing considerations <i>[Links to 1.1]</i></p> <p>Review the online training for prescribers > <i>[Launches slide show PDF or div layer]</i></p> <p>Report completion of training for TRUVADA for a PrEP indication <i>[link to UBC and external database to capture name, degree, address (street, city, state, zip) and specialty]</i></p> <p>Participate in a Knowledge, Attitude, and Behavior (KAB) survey to assess the use and understanding of TRUVADA for PrEP <i>[link to UBC for KAB pre-qualification page]</i></p>	<p>REMS Information</p> <p>A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure that the benefits of the drug outweigh its risks.</p> <p>To make sure TRUVADA for a PrEP indication is prescribed and taken safely, Gilead has worked with the FDA to develop materials for the REMS program to educate and inform healthcare providers and uninfected individuals at high risk for acquiring HIV-1.</p> <p>Access REMS resources > <i>[Links to 3.1]</i></p>
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Slide Show/Review Questions

Area on page	Description and copy
Slide 1	<p>TRUVADA[®] for a Pre-exposure Prophylaxis (PrEP) Indication Healthcare Provider Training</p>

<p>Slide 2</p>	<p>Pre-Exposure Prophylaxis (PrEP) Indication</p> <ul style="list-style-type: none"> • 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.
<p>Slide 3</p>	<p>Factors to Help Identify Individuals at High Risk</p> <ul style="list-style-type: none"> • Has partner known to be HIV-1 infected, <i>or</i> • Engages in sexual activity within a high prevalence area or social network and one or more of the following: <ul style="list-style-type: none"> – Inconsistent or no condom use – Diagnosis of sexually transmitted infections – Exchange of sex for commodities (such as money, shelter, food, or drugs) – Use of illicit drugs or alcohol dependence – Incarceration – Partner(s) of unknown HIV-1 status with any of the factors listed above
<p>Slide 4</p>	<p>When Prescribing TRUVADA for a PrEP Indication, Healthcare Providers MUST:</p> <ul style="list-style-type: none"> • 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 and recent (<1 month) exposures are suspected, <ul style="list-style-type: none"> – 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 • While using TRUVADA for a PrEP indication, HIV-1 screening tests should be repeated at least every 3 months <ul style="list-style-type: none"> – If symptoms consistent with acute HIV-1 infection develop following a potential exposure event, TRUVADA 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

<p>Slide 5</p>	<p>BOXED WARNING</p> <ul style="list-style-type: none"> • 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-1 infection are present unless negative infection status is confirmed.
<p>Slide 6</p>	<p>BOXED WARNING (Continued)</p> <ul style="list-style-type: none"> • 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.
<p>Slide 7</p>	<p>Why Use TRUVADA for a PrEP Indication?</p> <ul style="list-style-type: none"> • 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 <ul style="list-style-type: none"> – 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 infection

<p>Slide 8</p>	<p>Key Findings of the TRUVADA for a PrEP Indication Studies: The iPrEx Trial</p> <ul style="list-style-type: none"> • 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
<p>Slide 9</p>	<p>Key Findings of the TRUVADA for a PrEP Indication Studies: The Partners PrEP Trial</p> <ul style="list-style-type: none"> • In another clinical trial 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
<p>Slide 10</p>	<p>Important Safety Information: Comprehensive Management to Reduce the Risk of Acquiring HIV-1 Infection</p> <ul style="list-style-type: none"> • Prescribe TRUVADA for PrEP 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 <ul style="list-style-type: none"> – 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

<p>Slide 11</p>	<p>Important Safety Information: Comprehensive Management to Reduce the Risk of Acquiring HIV-1 Infection</p> <ul style="list-style-type: none"> • Prescribe TRUVADA to reduce the risk of acquiring HIV-1 infection only in individuals confirmed to be HIV-negative <ul style="list-style-type: none"> – 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 <ul style="list-style-type: none"> • 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 (e.g., fever, fatigue, myalgia, skin rash, etc.) and ask about potential exposure events (e.g., unprotected, or condom broke during sex with an HIV-1 infected partner) that may have occurred within the last month
<p>Slide 12</p>	<p>Important Safety Information: Comprehensive Management to Reduce the Risk of Acquiring HIV-1 Infection</p> <ul style="list-style-type: none"> • 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 and recent (<1 month) exposures are suspected, <ul style="list-style-type: none"> – 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 • While using TRUVADA for a PrEP indication, HIV-1 screening tests should be repeated at least every 3 months <ul style="list-style-type: none"> – 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
<p>Slide 13</p>	<p>Important Safety Information: Comprehensive Management to Reduce the Risk of Acquiring HIV-1 Infection</p> <p>Counsel uninfected individuals to strictly adhere to the recommended daily TRUVADA dosing schedule. The effectiveness of TRUVADA in reducing the risk of acquiring HIV-1 infection is strongly correlated with adherence and measurable drug levels</p>

<p>Slide 14</p>	<p>Important Safety Information: Additional Warnings and Precautions New Onset or Worsening Renal Impairment</p> <ul style="list-style-type: none"> • Can include acute renal failure and Fanconi syndrome • Assess estimated creatinine clearance (CrCl) before prescribing treatment with TRUVADA and periodically during therapy with TRUVADA • In individuals at risk of renal impairment, assess estimated CrCl, serum phosphorus, urine glucose and urine protein before prescribing TRUVADA and periodically while TRUVADA is being used
<p>Slide 15</p>	<p>Important Safety Information: Additional Warnings and Precautions New Onset or Worsening Renal Impairment</p> <ul style="list-style-type: none"> • 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 use TRUVADA for a PrEP indication in HIV-1 uninfected individuals with an estimated CrCl below 60 mL/min <ul style="list-style-type: none"> – If a decrease in estimated CrCl is observed in uninfected individuals while using TRUVADA for PrEP, evaluate potential causes and re-assess potential risks and benefits of continued use
<p>Slide 16</p>	<p>Important Safety Information: Additional Warnings and Precautions Bone effects</p> <ul style="list-style-type: none"> • 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

<p>Slide 17</p>	<p>Important Safety Information: Additional Warnings and Precautions</p> <p>Redistribution/accumulation of body fat</p> <ul style="list-style-type: none"> Observed in patients receiving antiretroviral therapy for treatment of HIV-1 infection <p>HBV Infection</p> <ul style="list-style-type: none"> It is recommended that all individuals be tested for the presence of chronic HBV before initiating TRUVADA HBV-uninfected individuals should be offered vaccination <p>Coadministration with other products</p> <ul style="list-style-type: none"> Do not use TRUVADA with drugs containing emtricitabine, tenofovir disoproxil fumarate, or tenofovir alafenamide, with drugs containing lamivudine, or with adefovir dipivoxil
<p>Slide 18</p>	<p>Important Safety Information: Use of TRUVADA for a PrEP Indication in Specific Populations</p> <p>Pregnancy</p> <ul style="list-style-type: none"> 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 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 <p>*Gray RH, et al. <i>Lancet</i>. 2005;366(9492):1182-1188.</p>
<p>Slide 19</p>	<p>Important Safety Information: Use of TRUVADA for a PrEP Indication in Specific Populations</p> <p>Nursing Mothers</p> <ul style="list-style-type: none"> The components of TRUVADA are excreted in breast milk. Because the risks to the infant are not known, mothers taking TRUVADA for PrEP 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 <p>Pediatrics</p> <ul style="list-style-type: none"> TRUVADA for a PrEP indication is based on trials in adults

<p>Slide 20</p>	<p>Important Safety Information: Confirming and Regularly Reconfirming Negative HIV-1 Status</p> <ul style="list-style-type: none"> • TRUVADA should be used to reduce the risk of acquiring HIV-1 infection only in individuals confirmed to be HIV-1 negative <ul style="list-style-type: none"> – 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
<p>Slide 21</p>	<p>Important Safety Information: Confirming and Regularly Reconfirming Negative HIV Status</p> <p>Potential for Resistance in Undetected Acute HIV-1 Infection</p> <ul style="list-style-type: none"> – 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 <ul style="list-style-type: none"> • 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
<p>Slide 22</p>	<p>Important Safety Information: Drug Interactions and Common Adverse Events</p> <p>Drug Interactions</p> <ul style="list-style-type: none"> • Coadministration of TRUVADA with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of tenofovir. • For further details about TRUVADA drug interactions, please see the Prescribing Information [link to PDF of PI] for TRUVADA <p>Common Adverse Reactions</p> <ul style="list-style-type: none"> • 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.

<p>Slide 23</p>	<p>Additional Educational Materials</p> <ul style="list-style-type: none"> • Agreement Form for Initiating TRUVADA for Pre-exposure Prophylaxis (PrEP) <ul style="list-style-type: none"> – 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 Pre-exposure Prophylaxis (PrEP) <ul style="list-style-type: none"> – 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 available from www.TRUVADAprereps.com or by filling out the postage paid, business reply card at the back of the Training Guide for Healthcare Providers
<p>Slide 24</p>	<p>Additional Educational Materials</p> <ul style="list-style-type: none"> • Additional educational materials can be reviewed and downloaded at www.TRUVADAprereps.com • Please confirm completion of training by going to www.TRUVADAprereps.com or by filling out the postage paid, business reply card at back of the Training Guide for Healthcare Providers • Gilead is conducting a survey to fulfill an FDA-required Risk Evaluation and Mitigation Strategy (REMS) program to assess prescribers' knowledge regarding important safety information associated with the use of TRUVADA for a PrEP indication. To participate, please go to www.TRUVADAprereps.com or fill out the postage paid, business reply card at the back of the Training Guide for Healthcare Providers
<p>Post-training screen</p>	<p>Assess Your Knowledge of TRUVADA for a PrEP Indication</p> <p>[Buttons]</p> <p>Go to review questions <i>[Advances to questions page/launches question 1]</i></p> <p>No thanks <i>[Advances to input screen for specialty/degree]</i></p> <p>Report completion of training for TRUVADA for a PrEP indication <i>[link to UBC and external database to capture name, degree, address (street, city, state, zip) and specialty]</i></p> <p>Participate in a knowledge, attitude, and behavior (KAB) survey to assess the use and understanding of TRUVADA for PrEP <i>[link to UBC for KAB pre-qualification page]</i></p>

<p>Question 1</p> <p>Correct answer: D</p>	<p>TRUVADA for a PrEP indication should be used only:</p> <ul style="list-style-type: none"> 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 infection 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 infection 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 <table border="1" data-bbox="597 646 1432 789"> <tr> <td data-bbox="597 646 971 789"> <p>Correct Next <i>[Advances to next screen]</i></p> </td> <td data-bbox="971 646 1432 789"> <p>Incorrect. Please try again. Try again <i>[Greys out selected wrong answer]</i></p> </td> </tr> </table>	<p>Correct Next <i>[Advances to next screen]</i></p>	<p>Incorrect. Please try again. Try again <i>[Greys out selected wrong answer]</i></p>
<p>Correct Next <i>[Advances to next screen]</i></p>	<p>Incorrect. Please try again. Try again <i>[Greys out selected wrong answer]</i></p>		
<p>Question 2</p> <p>Correct answer: B</p>	<p>Which of the following statements is false?</p> <ul style="list-style-type: none"> 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 infection through injection drug use c) Women taking TRUVADA for a PrEP indication should not breastfeed their babies d) TRUVADA for a PrEP indication is not always effective in preventing HIV-1 infection <table border="1" data-bbox="597 1167 1432 1310"> <tr> <td data-bbox="597 1167 971 1310"> <p>Correct Next <i>[Advances to next screen]</i></p> </td> <td data-bbox="971 1167 1432 1310"> <p>Incorrect. Please try again. Try again <i>[Greys out selected wrong answer]</i></p> </td> </tr> </table>	<p>Correct Next <i>[Advances to next screen]</i></p>	<p>Incorrect. Please try again. Try again <i>[Greys out selected wrong answer]</i></p>
<p>Correct Next <i>[Advances to next screen]</i></p>	<p>Incorrect. Please try again. Try again <i>[Greys out selected wrong answer]</i></p>		

<p>Question 3</p> <p>Correct answer: B</p>	<p>Which of the following items are not included on the Checklist for Prescribers for initiating TRUVADA for a PrEP indication?</p> <ul style="list-style-type: none"> 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 <table border="1" data-bbox="594 625 1432 802"> <tr> <td data-bbox="594 625 971 802"> <p>Correct</p> <p>Next <i>[Advances to next question]</i></p> </td> <td data-bbox="971 625 1432 802"> <p>Incorrect</p> <p>Try again <i>[Greys out selected wrong answer]</i></p> </td> </tr> </table>	<p>Correct</p> <p>Next <i>[Advances to next question]</i></p>	<p>Incorrect</p> <p>Try again <i>[Greys out selected wrong answer]</i></p>
<p>Correct</p> <p>Next <i>[Advances to next question]</i></p>	<p>Incorrect</p> <p>Try again <i>[Greys out selected wrong answer]</i></p>		
<p>Question 4</p> <p>Correct answer: A</p>	<p>Hepatic function should be monitored closely in:</p> <ul style="list-style-type: none"> a. HBV-infected individuals who discontinue TRUVADA b. All people taking TRUVADA c. All people who discontinue TRUVADA d. None of the above <table border="1" data-bbox="594 1180 1432 1320"> <tr> <td data-bbox="594 1180 971 1320"> <p>Correct</p> <p>Next <i>[Advances to next screen]</i></p> </td> <td data-bbox="971 1180 1432 1320"> <p>Incorrect. Please try again.</p> <p>Try again <i>[Greys out selected wrong answer]</i></p> </td> </tr> </table>	<p>Correct</p> <p>Next <i>[Advances to next screen]</i></p>	<p>Incorrect. Please try again.</p> <p>Try again <i>[Greys out selected wrong answer]</i></p>
<p>Correct</p> <p>Next <i>[Advances to next screen]</i></p>	<p>Incorrect. Please try again.</p> <p>Try again <i>[Greys out selected wrong answer]</i></p>		
<p>Question 5</p> <p>Correct answer: c</p>	<p>In clinical trials evaluating TRUVADA for a PrEP indication, which of the following adverse reactions was not common?</p> <ul style="list-style-type: none"> a) Abdominal pain b) Headache c) Dizziness d) Decreased weight <table border="1" data-bbox="594 1629 1432 1770"> <tr> <td data-bbox="594 1629 971 1770"> <p>Correct</p> <p>Next <i>[Advances to next screen]</i></p> </td> <td data-bbox="971 1629 1432 1770"> <p>Incorrect. Please try again.</p> <p>Try again <i>[Greys out selected wrong answer]</i></p> </td> </tr> </table>	<p>Correct</p> <p>Next <i>[Advances to next screen]</i></p>	<p>Incorrect. Please try again.</p> <p>Try again <i>[Greys out selected wrong answer]</i></p>
<p>Correct</p> <p>Next <i>[Advances to next screen]</i></p>	<p>Incorrect. Please try again.</p> <p>Try again <i>[Greys out selected wrong answer]</i></p>		

<p>Question 6</p> <p>Correct answer: D</p>	<p>TRUVADA for a PrEP indication is indicated only for:</p> <ul style="list-style-type: none"> 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 <table border="1" data-bbox="594 436 1432 579"> <tr> <td data-bbox="594 436 971 579"> <p>Correct</p> <p>Next</p> <p><i>[Advances to next screen]</i></p> </td> <td data-bbox="971 436 1432 579"> <p>Incorrect. Please try again.</p> <p>Try again</p> <p><i>[Greys out selected wrong answer]</i></p> </td> </tr> </table>	<p>Correct</p> <p>Next</p> <p><i>[Advances to next screen]</i></p>	<p>Incorrect. Please try again.</p> <p>Try again</p> <p><i>[Greys out selected wrong answer]</i></p>
<p>Correct</p> <p>Next</p> <p><i>[Advances to next screen]</i></p>	<p>Incorrect. Please try again.</p> <p>Try again</p> <p><i>[Greys out selected wrong answer]</i></p>		
<p>Question 7</p> <p>Correct answer: D</p>	<p>The Agreement Form for Initiating TRUVADA for Pre-exposure Prophylaxis (PrEP) provides which of the following information:</p> <ul style="list-style-type: none"> a. A list of activities that put individuals at risk for sexually acquired HIV-1 infection 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 <table border="1" data-bbox="594 1161 1432 1339"> <tr> <td data-bbox="594 1161 971 1339"> <p>Correct</p> <p><i>[Auto advances to resolve screen]</i></p> </td> <td data-bbox="971 1161 1432 1339"> <p>Incorrect</p> <p>Try again</p> <p><i>[Greys out selected wrong answer]</i></p> </td> </tr> </table>	<p>Correct</p> <p><i>[Auto advances to resolve screen]</i></p>	<p>Incorrect</p> <p>Try again</p> <p><i>[Greys out selected wrong answer]</i></p>
<p>Correct</p> <p><i>[Auto advances to resolve screen]</i></p>	<p>Incorrect</p> <p>Try again</p> <p><i>[Greys out selected wrong answer]</i></p>		

<p>Input screen</p>	<p>To help Gilead and the FDA understand who has viewed this training, please tell us the following</p> <p>Your Specialty:</p> <p style="padding-left: 40px;"><i>[drop down menu]</i></p> <p style="padding-left: 40px;">Internal medicine</p> <p style="padding-left: 40px;">Family practice</p> <p style="padding-left: 40px;">General medicine</p> <p style="padding-left: 40px;">Infectious diseases</p> <p style="padding-left: 40px;">Obstetrics/gynecology</p> <p style="padding-left: 40px;">Addiction medicine</p> <p style="padding-left: 40px;">Other</p> <p>Profession:</p> <p style="padding-left: 40px;"><i>[drop down menu]</i></p> <p style="padding-left: 40px;">MD</p> <p style="padding-left: 40px;">PA</p> <p style="padding-left: 40px;">NP</p> <p style="padding-left: 40px;">Other</p> <p>Zip Code: [insert box to capture 5 digit zip code]</p> <p>[Buttons]</p> <p>Submit <i>[Advances to thank you screen]</i></p> <p>No thanks <i>[Closes div layer]</i></p> <p style="padding-left: 40px;"><i>[one time error state if user misses a field on "Submit" only]</i></p> <p style="padding-left: 40px;">Please provide this information.</p> <p>Report completion of training for TRUVADA for a PrEP indication <i>[link to UBC and external database to capture name, degree, address (street, city, state, zip) and specialty]</i></p> <p>Participate in a Knowledge, Attitude, and Behavior (KAB) survey to assess the use and understanding of TRUVADA for PrEP <i>[link to UBC for KAB pre-qualification page]</i></p>
<p>Thank you screen</p>	<p><i>[H1]</i></p> <p>Thank you</p> <p>Close <i>[Closes div layer]</i></p>

1.1, About TRUVADA for a PrEP Indication

Area on page	Description and copy
Headline	About TRUVADA for a PrEP Indication
	<p>TRUVADA 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. The following factors may help to identify individuals at high risk:</p> <ul style="list-style-type: none"> • 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: <ul style="list-style-type: none"> – Inconsistent or no condom use – Diagnosis of sexually transmitted infections – Exchange of sex for commodities (such as money, shelter, food, or drugs) – Use of illicit drugs, alcohol dependence – Incarceration – Partner(s) of unknown HIV-1 status with any of the factors listed above
Copy	<p>When prescribing TRUVADA for pre-exposure prophylaxis, healthcare providers must:</p> <ul style="list-style-type: none"> • 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 TRUVADA daily dosing schedule because the effectiveness of TRUVADA in reducing the risk of acquiring HIV-1 infection was 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 • Be sure to not prescribe TRUVADA for a PrEP indication if signs or symptoms of acute HIV-1 infection are present

H2	Mechanism of action for pre-exposure prophylaxis
Copy	By inhibiting HIV-1 from replicating as it enters the body, TRUVADA for a PrEP indication helps prevent the virus from establishing permanent infection. TRUVADA for a PrEP indication does not replace existing HIV-1 prevention strategies.
Next page callout	Next: Comprehensive Management <i>[Links to 1.2]</i>

1.2. Comprehensive Management

Area on page	Description and copy
Headline	Comprehensive Management
Copy	<p>Prescribe TRUVADA for pre-exposure prophylaxis 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.</p> <ul style="list-style-type: none"> • Counsel uninfected individuals about safer sex practices that include consistent and correct use of condoms, limiting the number of sexual partners, 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 <p>Prescribe 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 treatment; therefore, care should be taken to minimize drug exposure in HIV-1 infected individuals.</p> <ul style="list-style-type: none"> ▪ Evaluate for signs or symptoms of acute HIV-1 infection prior to prescribing and while taking TRUVADA ▪ You must confirm a negative HIV-1 test immediately prior to prescribing TRUVADA for a PrEP indication. If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposures are suspected, delay starting TRUVADA for at least 1 month and reconfirm HIV-1 negative 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, 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 <p>Counsel uninfected individuals to strictly adhere to the recommended TRUVADA daily dosing schedule. The effectiveness of TRUVADA in reducing the risk of acquiring HIV-1 infection is strongly correlated with adherence and measurable drug levels.</p>
Bold copy	<p>It's important to remember that TRUVADA for a PrEP indication is contraindicated in individuals with unknown or positive HIV-1 status. TRUVADA should only be used in HIV-1 infected patients in combination with other antiretroviral agents.</p>

Copy	<p>Access tools that can help you manage and counsel individuals on the correct and safe use of TRUVADA for a PrEP indication.</p> <p>Checklist for Prescribers > <i>[Links to 2.1]</i></p> <p>Agreement form > <i>[Links to 2.2]</i></p>
Next page callout	<p>Next: Important Safety Information</p> <p><i>[Links to 1.3]</i></p>

1.3. Important Safety Information

Area on page	Description and copy
Headline	Important Safety Information
Copy	<p>Before prescribing TRUVADA for a PrEP indication, please review the complete Important Safety Information. To access a specific section of the Important Safety Information, use the links below:</p> <p>BOXED WARNING Warnings & Precautions Adverse Reactions Specific Populations Drug Interactions Indication</p>
Bold copy	<div style="border: 1px solid black; padding: 10px;"> <p>BOXED WARNING:</p> <ul style="list-style-type: none"> • TRUVADA for a PrEP indication must only be prescribed to individuals confirmed to be HIV-1 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 • 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 HBV-infected patients who discontinue TRUVADA. If appropriate, initiation of anti-hepatitis B therapy may be warranted </div>
Copy	<p>Contraindications: DO NOT PRESCRIBE TRUVADA for pre-exposure prophylaxis in individuals with unknown or positive HIV-1 status. TRUVADA should be used in HIV-1 infected patients only in combination with other antiretroviral agents.</p>
H3	<p>Warnings and Precautions Relating to the Use of TRUVADA for a PrEP Indication</p>

▪ **Comprehensive management strategies to reduce potential risks associated with use of TRUVADA for a PrEP indication:**

- **Strategy to reduce uninfected individual's exposure to HIV-1 infection** includes safer sex practices such as consistent and correct use of condoms, an individual knowing their HIV-1 status and that of their partner(s), regular testing for HIV-1 and other sexually transmitted infections, and counseling regarding reducing sexual risk behavior
- **Strategies to reduce potential for drug resistance: TRUVADA must only be used for PrEP 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 regimen for HIV-1 treatment
 - Confirm negative HIV-1 status immediately prior to initiating TRUVADA for PrEP. Do not initiate TRUVADA for PrEP if signs or symptoms of HIV-1 infection are present (e.g., fever, fatigue, myalgia, skin rash, etc.) or if recent exposure (<1 month) is suspected. Alternatively, delay initiating PrEP for at least one month or confirm negative HIV-1 status using 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 every three (3) months. Discontinue TRUVADA for PrEP if signs or symptoms of acute infection develop after potential exposure event until negative HIV-1 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
- Counsel all uninfected individuals to strictly adhere to their TRUVADA daily dosing schedule because the effectiveness of TRUVADA for PrEP is correlated with adherence and measurable drug levels

<p>Bullet list</p>	<ul style="list-style-type: none"> • New or worsening renal impairment: Acute renal impairment including Fanconi syndrome may occur. Assess estimated creatinine clearance (CrCl) before prescribing 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. 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. <ul style="list-style-type: none"> – 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 PrEP, 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 hepatitis B virus (HBV) before initiating TRUVADA. HBV-uninfected individuals should be offered vaccination • Bone effects: Consider assessment of bone mineral density (BMD) in individuals with history of bone fractures, 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 co-administer with other drugs containing emtricitabine, tenofovir disoproxil fumarate, or tenofovir alafenamide, with drugs containing lamivudine, or with adefovir dipivoxil
<p>H3</p>	<p>Common Adverse Reactions</p>
<p>Copy</p>	<p>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.</p>
<p>H3</p>	<p>Potential drug interactions: Coadministration of TRUVADA with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of tenofovir.</p> <p>Please see Prescribing Information for more information about potential drug interactions.</p>
<p>H3</p>	<p>Use of TRUVADA for PrEP in Specific Populations</p>

<p>Bullet list, please bold as shown</p>	<ul style="list-style-type: none"> ● 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 <ul style="list-style-type: none"> – 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 and 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. ● Pediatrics: The TRUVADA for a PrEP indication is based on studies in adults
<p>H3</p>	<p>Dosage and Administration</p>
<p>Bullet list, please bold as shown</p>	<ul style="list-style-type: none"> ● Adults: Dosage of TRUVADA for PrEP for adults is one tablet once per day orally with or without food ● Dose Adjustment for Renal Impairment: 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 PrEP, evaluate potential causes and re-assess potential risks and benefits of continued use
<p>H3</p>	<p>Indication and Usage for Pre-exposure Prophylaxis</p>

	<p>TRUVADA® (emtricitabine/tenofovir disoproxil fumarate), a combination of EMTRIVA® (emtricitabine) and VIREAD® (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.</p> <p><u>Factors that may help identify individuals at high risk include:</u> 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 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.</p> <p><u>The following points must be considered when prescribing TRUVADA for pre-exposure prophylaxis:</u></p> <ul style="list-style-type: none"> - 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 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 PrEP <p>Do not initiate TRUVADA for a PrEP indication if signs or symptoms of acute HIV-1 infection are present</p>
<p>Bold copy</p>	<p>Please report adverse events to Gilead by calling 1-800-445-3235. Adverse events can also be reported to the FDA through www.fda.gov/medwatch or by calling 1-800-FDA-1088. [Links to https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm]</p>
<p>Next page callout</p>	<p>Next: Checklist for Prescribers [Links to 2.1]</p>

2.1. Checklist for Prescribers

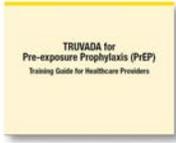
Area on page	Description and copy
Headline	Checklist for Prescribers
Copy	<p>Before prescribing TRUVADA for a PrEP indication, it's important that you complete the Checklist for Prescribers: Initiation of TRUVADA for Pre-Exposure Prophylaxis (PrEP) with uninfected individuals and file in the individual's medical record. <i>[Opens PDF download (TO COME) of checklist]</i> On each visit with an uninfected individual, complete the following steps:</p>
Copy	<ul style="list-style-type: none"> ▪ Complete high risk evaluation of uninfected individual ▪ Confirm a negative HIV-1 test immediately prior to initiating TRUVADA for a PrEP indication. <ul style="list-style-type: none"> ○ If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposure is 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 (Note: TRUVADA for a PrEP indication is contraindicated in individuals with unknown HIV-1 status or who are HIV-1 positive) • Discuss known safety risks with use of TRUVADA for a PrEP indication • Counsel on the importance of scheduled follow-up every 2 to 3 months including regular HIV-1 screening tests (at least every 3 months) while taking TRUVADA for PrEP to reconfirm HIV-1 status • Discuss the importance of discontinuing TRUVADA for a PrEP indication if seroconversion has occurred, to reduce the development of resistant HIV-1 variants • Counsel on the importance of adherence to daily dosing schedule • Counsel that TRUVADA for a PrEP indication should be used only as part of a comprehensive prevention strategy • Educate on practicing safer sex consistently and using condoms correctly • Discuss the importance of the individual knowing their HIV-1 status and, if possible, that of their partner(s) • Discuss the importance of and perform screening for sexually transmitted infections (STIs), such as syphilis and gonorrhea, that can facilitate HIV-1 transmission

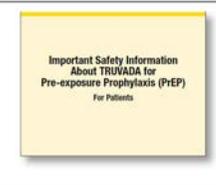
	<ul style="list-style-type: none"> ▪ Perform HBV screening test. Offer HBV vaccination as appropriate ▪ Confirm estimated creatinine clearance (CrCl) ≥ 60 mL/min prior to initiation and periodically during treatment. In patients at risk for renal dysfunction, assess estimated creatinine clearance, serum phosphorus, urine glucose and urine protein before initiation of TRUVADA and periodically while TRUVADA is being used. If a decrease in estimated CrCl is observed in uninfected individuals while using TRUVADA for PrEP, evaluate potential causes and re-assess potential risks and benefits of continued use ▪ Confirm that the uninfected individual at high risk is not taking other HIV-1 medications or hepatitis B medications ▪ Provide education on where information about TRUVADA for a PrEP indication can be accessed ▪ Discuss potential adverse events ▪ Review the TRUVADA Medication Guide with the uninfected individual at high risk <i>[Links to http://www.truvadapreprems.com/pdf/fpi.pdf]</i> ▪ Evaluate risk/benefit for women who may be pregnant or may want to become pregnant
<p>Next page callout</p>	<p>Next: Agreement Form <i>[Links to 2.2]</i></p>

2.2. Agreement Form

Area on page	Description and copy
Headline	Agreement Form
Copy	As part of helping uninfected individuals understand the commitment in taking TRUVADA for a PrEP indication, the Agreement Form for Initiating TRUVADA for Pre-exposure Prophylaxis (PrEP) has been created. It's important that you use the form to review the factors that may help to identify uninfected individuals at high risk. These include:
Copy	<ul style="list-style-type: none"> ▪ Has partner(s) known to be HIV-1 infected, <i>or</i> ▪ Engages in sexual activity within a high prevalence area or social network and one or more of the following: <ul style="list-style-type: none"> - Inconsistent or no condom use - Diagnosis of sexually transmitted infections - Exchange of sex for commodities (such as money, shelter, food, or drugs) - Use of illicit drugs, alcohol dependence - Incarceration - Partner(s) of unknown HIV-1 status with any of the factors listed above
Copy	After you review the risks and benefits with the individual, you must both sign and date the form and file in the individual's medical record. This will help to reinforce the importance of understanding the risks involved with TRUVADA for a PrEP indication. Download a printable version of the Agreement Form. <i>[Opens PDF download (TO COME) of checklist]</i>
Next page callout	Next: REMS Materials <i>[Links to 3.1]</i>

3.1, REMS Materials

Area on page	Description and copy	
Headline	REMS Materials	
Copy	On this page, you'll find downloadable resources for you and uninfected individuals. You will need Adobe Acrobat installed on your computer to view these resources. If you do not have it and would like to download it, please click here . <i>[Links to http://get.adobe.com/reader]</i>	
H3	<i>Dear Healthcare Provider Letter</i>	
Download box	 <p style="text-align: center;">FOR POSITION ONLY</p>	Information for healthcare providers on the new TRUVADA indication for pre-exposure prophylaxis (PrEP) Download <i>[Links to PDF download]</i>
H3	<i>Training Guide for Healthcare Providers</i>	
Download box		A comprehensive overview of TRUVADA for a PrEP indication Download <i>[Links to PDF download]</i>
H3	<i>Important Safety Information for Healthcare Providers</i>	
Download box		Important safety information about TRUVADA for a PrEP indication Download <i>[Links to PDF download]</i>
H3	<i>Safety Information Fact Sheet</i>	
Download box	 <p style="text-align: center;">FOR POSITION ONLY</p>	A detailed overview of the safety information for TRUVADA for a PrEP indication Download <i>[Links to PDF download]</i>

H3	<i>Agreement Form for Initiating TRUVADA for Pre-Exposure Prophylaxis (PrEP)</i>	
Download box		Form that should be reviewed with an individual considering/taking TRUVADA for a PrEP indication Download <i>[Links to PDF download]</i>
H3	<i>Checklist for Prescribers: Initiation of TRUVADA for Pre-Exposure Prophylaxis (PrEP)</i>	
Download box		Tool for facilitating appropriate prescribing of TRUVADA for a PrEP indication Download <i>[Links to PDF download]</i>
H3	<i>Medication Guide</i>	
Download box		A comprehensive guide for uninfected individuals getting started on TRUVADA for a PrEP indication Download <i>[Links to http://www.truvadapreprems.com/pdf/fpi.pdf]</i>
H3	<i>Important Safety Information about TRUVADA to Reduce the Risk of Getting Human Immunodeficiency Virus-1 (HIV-1) Infection</i>	
Download box		An easy-to-understand guide on the most important safety information about TRUVADA for a PrEP indication Download <i>[Links to PDF download]</i>
H3	Full <i>Prescribing Information</i>	
Download box		Prescribing Information for TRUVADA for a PrEP indication Download <i>[Links to http://www.truvadapreprems.com/pdf/fpi.pdf]</i>
Next page callout	Next: Post-Training Review Questions <i>[Links to 3.2]</i>	

3.2, Post-Training Review Questions

Area on page	Description and copy
Headline	Post-Training Review Questions
Copy	If you are a healthcare provider considering prescribing TRUVADA for a PrEP indication, assess your knowledge about the safe use of TRUVADA for a PrEP indication.
Copy	<p>Go to review questions <i>[Launches first question]</i></p> <p>Report completion of training for TRUVADA for a PrEP indication <i>[link to UBC and external database to capture name, degree, address (street, city, state, zip) and specialty]</i></p> <p>Participate in a knowledge, attitude, and behavior (KAB) survey to assess the use and understanding of TRUVADA for PrEP <i>[link to UBC for KAB pre-qualification page]</i></p>

Div layer for first time visit

Area on page	Description and copy
Copy	The information on this site is intended for adult residents of the United States.
Buttons	OK <i>[Continues to site]</i>

5.0, Site Map

Area on page	Description and copy
Headline	Site Map
Copy	<p>Home [Links to 0.0 <i>www.TruvadaPrEPprems.com</i>]</p> <p>Prophylaxis Therapy [Links to 1.1] TRUVADA for a PrEP Indication [Links to 1.1] Comprehensive Management [Links to 1.2] Important Safety Information [Links to 1.3]</p> <p>Starting Individuals [Links to 2.1] Checklist for Prescribers [Links to 2.1] Agreement Form</p> <p>Support [Links to 3.1] REMS Materials [Links to 3.1] Post-Training Review Questions [Links to 3.2]</p>

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JEFFREY S MURRAY
03/10/2016