Initial REMS Approval: 07/16/2012

Supplemental NDA 21-752

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, other healthcare professionals, and 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. Medication Guide

A TRUVADA Medication Guide will be dispensed with each TRUVADA prescription in accordance with 21 CFR 208.24.

The Medication Guide is part of the REMS and is appended.

B. Elements to Assure Safe Use

1. Gilead Sciences, Inc., will ensure that training and education through the TRUVADA for a PrEP Indication Healthcare Professional Education Program is available to healthcare providers who prescribe TRUVADA for a PrEP indication.

    a. Gilead will ensure that training and education materials will be available for completion by healthcare providers who prescribe TRUVADA for a PrEP indication via the TRUVADA for a PrEP Indication Healthcare Professional Education Program online via the REMS Website (www.TRUVADApreprems.com) or by print training modules available as hard copy, upon request. This information will remain on the REMS website for a period of 3 years from initial approval.

    b. Gilead's training efforts will target the following healthcare providers 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

    c. 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 for outreach to healthcare providers likely to prescribe TRUVADA for a PrEP indication as described in b. above.

        i. The Safety Information Fact Sheet will be available for distribution via online access or printed hard copy for select professional organizations to disseminate to healthcare providers bi-annually, for 3 years.

        ii. The Safety Information Fact Sheet 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 & County Health Officials
- American College of Preventive Medicine
- National Association of Public Hospitals
- American Pharmacists Association

The Safety Information Fact Sheet will be provided to MedWatch at the same time it is provided to these professional organizations.

The Safety Information Fact Sheet is appended and part of the REMS.

d. 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 healthcare providers 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 appended and part of the REMS

e. Gilead will ensure that, as part of training and education, the following materials are available to healthcare providers:

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 healthcare professionals who are likely to prescribe TRUVADA for a PrEP indication, as described in b. 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 full Prescribing Information and Medication Guide will also be available with the DHCP letter. The letter will be available via a REMS-specific link from the TRUVADA REMS website (www.TRUVADApreprems.com) on the date of the first mailing.

Gilead will distribute the DHCP letter to the targeted healthcare providers 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 for a PrEP Indication for Uninfected Individuals** 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) of Sexually Acquired HIV-1 Infection** 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** as a reminder for the management of an 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 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 Professional Training and Education Program Kit which will consist of the following materials to support the training and educational process:

1. Full Prescribing Information
2. Medication Guide
3. Dear Healthcare Provider Letter
4. Training Guide for Healthcare Providers
5. Prescriber Educational Slide Deck
6. Important Safety Information about TRUVADA for a PrEP Indication for Healthcare Providers

7. Important Safety Information about TRUVADA for a PrEP Indication for Uninfected Individuals

8. Agreement Form for Initiating TRUVADA for Pre-Exposure Prophylaxis of Sexually Acquired HIV-1 Infection for an uninfected individual taking TRUVADA for a PrEP indication

9. Checklist for Prescribers to manage an individual considering or taking TRUVADA for a PrEP indication

10. Safety Information Fact Sheet

These materials are part of the REMS and are appended.

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

C. 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. 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.

Medication Guide
TRUVADA ® (tru-VAH-dah)
(emtricitabine and tenofovir disoproxil fumarate)
Tablets

Read this Medication Guide before you start taking TRUVADA and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

What is the most important information I should know about TRUVADA?

TRUVADA can cause serious side effects, including:

1. Build-up of an acid in your blood (lactic acidosis). Lactic acidosis is a serious medical emergency that can lead to death.

Lactic acidosis can be hard to identify early, because the symptoms could seem like symptoms of other health problems. **Call your healthcare provider right away if you get the following symptoms which could be signs of lactic acidosis:**

- feeling very weak or tired
- unusual muscle pain
- trouble breathing
- stomach pain with
    - nausea
    - vomiting
- feel cold, especially in your arms and legs
- feel dizzy or lightheaded
- have a fast or irregular heartbeat

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 (hepatomegaly) and you may develop fat in your liver (steatosis) when you take TRUVADA. **Call your healthcare provider right away if you get the following symptoms:**

- your skin or the white part of your eyes turns yellow (jaundice)
- dark “tea-colored” urine
- light-colored bowel movements (stools)
- loss of appetite for several days or longer
- nausea
- stomach pain

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

3. Worsening of your hepatitis B infection. If you have hepatitis B virus (HBV) infection it may become worse (flare-up) if you take TRUVADA and then stop it. A “flare-up” is when your HBV infection suddenly returns in a worse way than before.

- Do not run out of TRUVADA. Refill your prescription or talk to your healthcare provider before your TRUVADA is all gone.

- Do not stop taking TRUVADA without first talking to your healthcare provider.
- If you stop taking TRUVADA, your healthcare provider will need to check your health often and do blood tests regularly for several months to check your HBV infection. Tell your healthcare provider about any new or unusual symptoms you may have after you stop taking TRUVADA.

For more information about side effects, see the section **"What are the possible side effects of TRUVADA?"**

Before taking TRUVADA to help prevent you from getting HIV:

- **You must get tested to be sure you are HIV-negative**. It is important that you also get tested at least every 3 months as recommended by your healthcare provider while taking TRUVADA. **Do not take TRUVADA to reduce the risk of getting HIV unless you are confirmed to be HIV-negative.**
- Tell your healthcare provider if you have any of the following symptoms within the last month before you start taking TRUVADA or at any time while taking TRUVADA:
  - tiredness
  - fever
  - sweating a lot (especially at night)
  - rash
  - vomiting
  - diarrhea
  - joint or muscle aches
  - headache
  - sore throat
  - enlarged lymph nodes in the neck or groin

  These may be signs of HIV infection and you may need to have a different kind of test to diagnose HIV. Also, tell your healthcare provider if you think you were exposed to the HIV virus. If you are already taking TRUVADA to prevent HIV-1 infection, your healthcare provider may tell you to stop taking TRUVADA until an HIV test confirms that you do not have HIV-1 infection.
- **TRUVADA by itself is not a complete treatment for HIV**. If you already have HIV or get HIV and take TRUVADA by itself without other medicines, you may develop resistance to TRUVADA. This means that the HIV virus may become harder to treat.
- **Just taking TRUVADA may not keep you from getting HIV**. **TRUVADA does not always prevent HIV.**
- **You must still practice safer sex at all times**. **Do not have any kind of sex without protection**. Always practice safer sex by using a latex or polyurethane condom to lower the chance of sexual contact with semen, vaginal secretions, or blood.
- **You must also use other prevention methods to keep from getting HIV.**
  - Know your HIV status and the HIV status of your partners. While taking TRUVADA, get tested at least every 3 months for HIV, as recommended by your healthcare provider. Ask your partners to get tested.
  - Get tested for other sexually transmitted infections such as syphilis and gonorrhea. These infections make it easier for HIV to infect you.
  - Get information and support to help reduce risky sexual behavior.
  - Have fewer sex partners.

- **Do not miss any doses of TRUVADA. Missing doses increases your risk of getting HIV.**
- **See the section "What is TRUVADA?" and talk to your healthcare provider for more information about how to prevent HIV infection.**

What is TRUVADA?

TRUVADA contains the prescription medicines emtricitabine (EMTRIVA®) and tenofovir disoproxil fumarate (VIREAD®). TRUVADA is used:

- with other antiviral medicines to treat Human Immunodeficiency Virus-1 (HIV-1) in adults and children age 12 years and older. HIV is the virus that causes AIDS (Acquired Immune Deficiency Syndrome).
- **with safer sex practices at all times,** to reduce the risk of getting HIV-1 in men who have sex with men who are at high risk of getting infected with HIV-1 through sex, and heterosexual couples where one partner has HIV-1 and the other does not. This is called Pre-Exposure Prophylaxis or PrEP.

It is not known if TRUVADA is safe and effective in children with HIV-1 infection who are under 12 years of age or who weigh less than 77 pounds.

When used with other HIV medicines to treat HIV-1 infection, TRUVADA may help:

- Reduce the amount of HIV in your blood. This is called "viral load."
- Increase the number of CD4+ (T) cells in your blood that help fight off other infections.
- Reducing the amount of HIV and increasing the CD4+ (T) cells in your blood may help improve your immune system. This may reduce your risk of death or infections that can happen when your immune system is weak (opportunistic infections).

TRUVADA does not cure HIV infection or AIDS. If you have HIV infection, you must stay on continuous HIV therapy to control HIV infection and decrease HIV-related illnesses.

Avoid doing things that can increase your risk of getting HIV infection or spreading HIV infection to other people:

- Do not share or re-use needles or other injection equipment.
- Do not share personal items that can have blood or body fluids on them, like toothbrushes and razor blades.
- Do not have any kind of sex without protection. Always practice safer sex by using a latex or polyurethane condom to lower the chance of sexual contact with semen, vaginal secretions, or blood.

Ask your healthcare provider if you have any questions on how to prevent getting HIV infection or spreading HIV infection to other people.

Who should not take TRUVADA?

Do not take TRUVADA to prevent HIV infection if you are HIV positive or if your HIV status is not known.

What should I tell my healthcare provider before taking TRUVADA?

See "What is the most important information I should know about TRUVADA?"

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 baby.

  If you are a female who is taking TRUVADA to prevent HIV infection and you become pregnant while taking TRUVADA, talk to your healthcare provider about whether you will continue taking TRUVADA.

  Pregnancy Registry. There is a pregnancy registry for women who take antiviral medicines during pregnancy. The purpose of this registry is to collect information about the health of you and your baby. Talk to your healthcare provider about how you can take part in this registry.
- are breastfeeding or plan to breastfeed. Do not breastfeed if you take TRUVADA.
  - You should not breastfeed if you have HIV because of the risk of passing HIV to your baby.
  - TRUVADA can pass to your baby in your breast milk.

  Talk with your healthcare provider about the best way to feed your baby.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. TRUVADA may affect the way other medicines work, and other medicines may affect how TRUVADA works.

Do not take TRUVADA if you also take:

- other medicines that contain tenofovir or emtricitabine (ATRIPLA, COMPLERA, EMTRIVA, VIREAD)
- medicines that contain lamivudine (Combivir, Epivir, Epivir-HBV, Epzicom, Trizivir)
- adefovir (HEPSERA)

Especially tell your healthcare provider if you take:

- didanosine (VIDEX EC)
- atazanavir (REYATAZ)
- lopinavir with ritonavir (KALETRA)

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

How should I take TRUVADA?

- Take TRUVADA exactly as prescribed.
- **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.
- TRUVADA is usually taken 1 time each day. If you have kidney problems, your healthcare provider may tell you to take TRUVADA less often.
- **When used to treat HIV-1 infection, TRUVADA is always used with other HIV-1 medicines.**
- **If you take TRUVADA to reduce the risk of getting HIV-1, you must also use other methods to reduce your risk of getting HIV. See "What is the most important information I should know about TRUVADA?"**
- Take TRUVADA by mouth, with or without food.
- Take TRUVADA at the same time each day.
- 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.
- It is important that you do not miss any doses of TRUVADA or your other HIV-1 medicines.
- When your TRUVADA supply starts to run low, get more from your healthcare provider or pharmacy. This is very important because the amount of virus in your blood may increase if the medicine is stopped for even a short time. The virus may develop resistance to TRUVADA and become harder to treat.
- If you take too much TRUVADA, call your healthcare provider or go to the nearest hospital emergency room right away.

What are the possible side effects of TRUVADA?

TRUVADA may cause the following serious side effects, including:

- **See "What is the most important information I should know about TRUVADA?"**
- **New or worse kidney problems,** including kidney failure. If you have had kidney problems in the past or need to take another medicine that can cause kidney problems, your healthcare provider may need to do blood tests to check your kidneys before you start and while you are taking TRUVADA. Your healthcare provider may tell you to take TRUVADA less often, or to stop taking TRUVADA if you have kidney problems.
- **Bone problems** can happen in some people who take TRUVADA. Bone problems include bone pain, softening or thinning (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**. These changes may include increased amount of fat in the upper back and neck ("buffalo hump"), breast, and around the middle of your body (trunk). Loss of fat from the legs, arms, and face may also happen. The exact cause and long-term health effects of these problems are not known.

- **Changes in your immune system (Immune Reconstitution Syndrome)** can happen when an HIV-infected person starts taking HIV medicines. Your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time. Tell your healthcare provider right away if you start having any new symptoms after starting your HIV medicine.

The most common side effects of TRUVADA in people with HIV-1 infection include:

- Diarrhea
- nausea
- tiredness
- headache
- dizziness
- depression
- problems sleeping
- abnormal dreams
- rash

Common side effects in people who take TRUVADA to prevent HIV-1 infection include:

- stomach-area (abdomen) pain
- headache
- decreased weight

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

These are not all 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 report side effects to FDA at 1-800-FDA-1088.

How should I 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.

General information about TRUVADA.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use TRUVADA for a condition for which it was not prescribed. Do not give TRUVADA to other people, even if they have the same symptoms you have. It may harm them.

This Medication Guide summarizes the most important information about TRUVADA. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about TRUVADA that is written for health professionals. For more information, call 1-800-445-3235 or go to www.TRUVADA.com.

What are the ingredients in TRUVADA?

Active ingredients: emtricitabine and tenofovir disoproxil fumarate

Inactive ingredients: Croscarmellose sodium, lactose monohydrate, magnesium stearate, microcrystalline cellulose, and pregelatinized starch (gluten free). The tablets are coated with Opadry II Blue Y-30-10701 which contains FD&C Blue #2 aluminum lake, hydroxypropyl methylcellulose 2910, lactose monohydrate, titanium dioxide, and triacetin.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured for and distributed by:
Gilead Sciences, Inc.
Foster City, CA 94404

Issued July 2012

21-752-GS-025

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 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 PrEP. 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
  - **– 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 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 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

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

GILEAD

Truvada®
200 mg emtri i i i i il fumarat 300 mg

Reference ID: 3159388

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 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 PrEP. 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

  – 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 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 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

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

GILEAD

Truvada®
200 mg emtri i i i i il fumarat 300 mg

Reference ID: 3159388

IMPORTANT DRUG WARNING

Subject: FDA-Required Risk Evaluation Mitigation Strategy (REMS) for a new indication 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. 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 a new indication for TRUVADA (a fixed-dose combination of emtricitabine 200 mg and tenofovir disoproxil fumarate 300 mg), approved by the FDA on July 16, 2012, for pre-exposure prophylaxis (PrEP) in combination with safer sex practices 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 FDA has determined that a Risk Evaluation Mitigation Strategy (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:

1. To inform and educate prescribers, other healthcare providers (HCPs), 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 obtain 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 fatigue, fever, sweating, pain, rash, diarrhea or coughing 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 of Sexually Acquired HIV-1 Infection** with an uninfected individual considering or taking TRUVADA for a PrEP indication and refer to the **Checklist for Prescribers** regarding the management of an uninfected individual taking TRUVADA for a PrEP indication. (*Access **Agreement Form** and **Checklist** via www.truvadapreprems.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 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 daily oral regimen

Management of Uninfected Individuals

Uninfected individuals at high risk should:

- Be counseled 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.
- 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 fatigue, sweating a lot (especially at night), rash, vomiting, diarrhea, joint or muscle aches, headache, sore throat, or enlarged lymph nodes in their neck or groin.
- Be screened at least every 3 months for HIV-1 as determined by their prescriber to confirm that they are HIV-1-negative while taking TRUVADA for a PrEP indication to reduce the risk of acquiring HIV-1.
- Have their creatinine clearance calculated prior to initiating TRUVADA, and not receive TRUVADA for a PrEP indication if creatinine clearance is <60 mL/min. If a decrease in creatinine clearance is observed in uninfected individuals while using TRUVADA for PrEP, the prescriber should evaluate potential causes and 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.

- 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 (including nausea, vomiting, unusual or unexpected stomach discomfort, and weakness)
- Be informed that TRUVADA has only been evaluated in a limited number of women during pregnancy and postpartum. Available human and animal data suggest that TRUVADA does not increase the risk of major birth defects overall compared to the background rate. There are, however, no adequate and well-controlled trials in pregnant women. Because the studies in humans cannot rule out the possibility of harm, TRUVADA should be used during pregnancy only if clearly needed. If an uninfected individual becomes pregnant while taking TRUVADA for a PrEP indication, careful consideration should be given to whether use of TRUVADA should be continued, taking into account the potential increased risk of HIV-1 infection during pregnancy.

REMS Website *(www.truvadapreprems.com)*

The REMS website provides access to the following:

- Specific information regarding the risks of TRUVADA for a PrEP indication
- Training and educational materials for prescribers that include safety information for uninfected individuals considering or taking TRUVADA for a PrEP indication, including the **Agreement Form for Initiating TRUVADA for Pre-Exposure Prophylaxis of Sexually Acquired HIV-1 Infection** and **Checklist for Prescribers**.

Reporting Adverse Events

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

- Gilead Pharmaceuticals, 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 Full Prescribing Information and Medication Guide for a complete description of safety risks.

Sincerely,

XXXXXX

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

For Healthcare Providers

Reference ID: 3159388

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

TRUVADA Safety Profile

WARNINGS: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS, POST-TREATMENT ACUTE EXACERBATION OF HEPATITIS B, and RISK OF DRUG RESISTANCE WITH USE OF TRUVADA FOR PRE-EXPOSURE PROPHYLAXIS (PrEP) 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 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**

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- **TRUVADA is not approved for the treatment of chronic hepatitis B virus (HBV) infection. Severe acute exacerbations of hepatitis B have been reported in patients coinfected with HIV-1 and HBV who have discontinued TRUVADA. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who are infected with HBV and discontinue TRUVADA. If appropriate, initiation of anti-hepatitis B therapy may be warranted**

Important Safety Information About TRUVADA for a PrEP Indication

Contraindication: 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**

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.

– Counsel uninfected individuals at high risk about safer sex practices, including:
  - Using condoms consistently and correctly
  - Knowing their HIV-1 status and that of their partner(s)
  - Being tested for other sexually transmitted infections
  - 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 only in individuals confirmed to be HIV-1 negative.** HIV-1 resistance substitutions may emerge in individuals with undetected HIV-1 infection who are taking only TRUVADA because TRUVADA alone does not constitute a complete treatment regimen for HIV-1 infection
  - Confirm a negative HIV-1 test immediately prior to initiating TRUVADA for a PrEP indication. 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
  - 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
  - Evaluate for signs or symptoms of acute HIV-1 infection prior to and while prescribing TRUVADA for a PrEP indication

– 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 detectable drug levels

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

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

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

  – HBV-uninfected individuals should be offered vaccination

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- **Decreases in bone mineral density (BMD):** Consider assessment of BMD in individuals with a history of pathologic fracture or other risk factors for osteoporosis or bone loss
- **Redistribution/accumulation of body fat:** Observed in patients receiving antiretroviral therapy
- **Immune reconstitution syndrome:** May necessitate further evaluation and treatment in patients with HIV-1 infection

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 confirmed on a regular basis (at least every 3 months) using HIV-1 screening tests while uninfected individuals are taking TRUVADA as part of a pre-exposure prophylaxis strategy.

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 weight decreased
- The most common adverse reactions (incidence greater than or equal to 10%) in HIV-1–infected patients are diarrhea, nausea, fatigue, headache, dizziness, depression, insomnia, abnormal dreams, and rash

Use of TRUVADA for a PrEP Indication in Specific Populations

- **Pregnancy:** There are no adequate and well-controlled trials in pregnant women. TRUVADA should be used during pregnancy only if clearly needed. If an uninfected individual becomes pregnant while taking TRUVADA for a PrEP indication, careful consideration should be given to whether use of TRUVADA should be continued, taking into account the potential increased risk of HIV-1 infection during pregnancy
  - A pregnancy registry is available. Enroll women taking TRUVADA for a PrEP indication by calling 1-800-258-4263
- **Nursing mothers:** Women infected with HIV-1 or taking TRUVADA for a PrEP indication should be instructed not to breast-feed. The components of TRUVADA (emtricitabine/tenofovir disoproxil fumarate) are excreted in breast milk, and the risk to the infant is not known
- **Pediatrics:** The TRUVADA for a PrEP indication is based on trials in adults

TRUVADA Drug Interactions

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

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

Use the Checklist for Prescribers and the Agreement Form 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 Full Prescribing Information, including Boxed WARNINGS, and Medication Guide. For more information about the REMS program for TRUVADA for a PrEP indication, please log on to www.TRUVADApreprems.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; 2012.

Reference ID: 3159388

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

For Uninfected Individuals

Reference ID: 3159388

TRUVADA for a PrEP indication

TRUVADA (emtricitabine/tenofovir disoproxil fumarate) is a medicine used in combination with safer sex practices to decrease the chance of getting HIV-1 in adults who are at high risk of getting infected with HIV-1 through sex.

TRUVADA is also used with other antiviral medicines to treat HIV-1 in adults and children 12 years and older.

Only take TRUVADA as part of a complete prevention strategy because TRUVADA is not always effective in preventing a person from getting infected with HIV-1.

What is the most important information you should know about taking TRUVADA?

TRUVADA can cause serious side effects. Some of these side effects are:

1. **Build-up of lactic acid in your blood (lactic acidosis).** This is a serious medical emergency that can lead to death. Lactic acidosis can be hard to identify early because the symptoms could seem like symptoms of other health problems. **Call your healthcare provider right away if you get these symptoms. They could be signs of lactic acidosis:**
   - Feeling very weak or tired
   - Unusual muscle pain
   - Trouble breathing
   - Stomach pain with nausea and/or vomiting
   - Feeling cold, especially in your arms and legs
   - Feeling dizzy or lightheaded
   - Having a fast or irregular heartbeat

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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 (hepatomegaly), and you may develop fat in your liver (steatosis) when you take TRUVADA. **Call your healthcare provider right away if you get these symptoms:**
   - Your skin or the white part of your eyes turns yellow (jaundice)
   - Dark "tea-colored" urine
   - Light-colored bowel movements (stools)
   - Loss of appetite for several days or longer
   - Nausea
   - Stomach pain

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

3. **Worsening of hepatitis B (HBV) infection.** If you have HBV infection, it may flare up and get worse if you take TRUVADA and then stop it. A flare-up is when your HBV infection suddenly comes back worse than before.
   - Do not run out of TRUVADA. Refill your prescription before your TRUVADA is all gone
   - Do not stop taking TRUVADA without first talking to your healthcare provider
   - If you stop taking TRUVADA, your healthcare provider will need to check your health often. Your healthcare provider will also need to do regular blood tests for several months to check your HBV infection

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

4. **You should not take TRUVADA for a PrEP indication if you are HIV-1 positive or do not know your status**

Before starting TRUVADA for a PrEP indication

You must be HIV-1 negative and stay HIV-1 negative **before** starting TRUVADA for a PrEP indication. That is why you **must:**

- Get tested to be sure you are HIV-1 negative. It is important that you also get tested at least every 3 months as recommended by your healthcare provider while taking TRUVADA
- Not take TRUVADA to reduce the risk of getting HIV unless you are confirmed to be HIV-1 negative
- Have no symptoms like feeling weak or tired, fever, sweating a lot (especially at night), rash, vomiting, diarrhea, joint or muscle aches, headache, sore throat, or enlarged lymph nodes in your neck or groin
- Be prepared to commit to adopting safer sex practices, such as regular and correct use of condoms, limiting your number of sexual partners, knowing the HIV status of your sexual partners, and regular testing for HIV-1 (at least every 3 months) and other sexually transmitted infections, such as syphilis and gonorrhea
- Make sure you understand the risks and benefits of taking TRUVADA for a PrEP indication as outlined in the TRUVADA Medication Guide and in the Agreement Form, and you have spoken with your healthcare provider about questions and concerns

After starting TRUVADA for a PrEP indication

Just taking TRUVADA may not keep you from getting HIV-1.
TRUVADA does not always prevent HIV-1.

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Here are some things you must do **after** starting TRUVADA for a PrEP indication:

- You will need to get tested regularly for HIV-1 to make sure that you are still HIV-1 negative. Your healthcare provider will tell you when
- Tell your healthcare provider if you have any of these symptoms: feeling weak or tired, fever, sweating a lot (especially at night), rash, vomiting, diarrhea, joint or muscle aches, headache, sore throat, or enlarged lymph nodes in your neck or groin. These may be signs of HIV-1 infection
- You must still practice safer sex at all times
  - Do not have any kind of sex without protection. Always practice safer sex by using a latex or polyurethane condom to lower the chance of sexual contact with semen, vaginal secretions, or blood
- You must also use other methods to keep from getting HIV-1:
  - Know your HIV-1 status and the HIV-1 status of your partner(s)
  - Get tested regularly for HIV-1. Ask your partner(s) to get tested
  - Get tested for other sexually transmitted infections, such as syphilis and gonorrhea. These infections make it easier for HIV-1 to infect you
  - Do not have risky sex
  - Have fewer sex partners
  - Do not share needles or other drug injection equipment
  - Do not share personal things, like toothbrushes and razors. They can have blood or body fluids on them
- **Do not miss any doses of TRUVADA. Missing doses raises the risk of getting HIV-1.** TRUVADA for a PrEP indication may not help you decrease the chance of getting HIV-1 if you do not take it exactly as prescribed. Be sure to stick to the TRUVADA daily dosing schedule
- **TRUVADA by itself is not a complete treatment for HIV-1.** If you already have HIV-1 or get HIV-1 and take TRUVADA by itself without other anti–HIV-1 medicines, you may develop resistance to TRUVADA
- TRUVADA needs to be in your blood to work. You may have to take TRUVADA for a few days before there is enough in your blood for it to help decrease your chance of getting HIV-1. Even after it is in your blood, it is still very important to practice safer sex

TRUVADA for a PrEP indication was tested in adults who were at high risk for getting infected with HIV-1 through sex.

When you should not take TRUVADA for a PrEP indication

Do not take TRUVADA to help prevent HIV-1 infection...

- If you have been tested for HIV-1 and have found out you are infected
- If you are already taking ATRIPLA® (efavirenz/emtricitabine/tenofovir disoproxil fumarate), COMPLERA® (emtricitabine/rilpivirine/tenofovir disoproxil fumarate), Combivir® (lamivudine/zidovudine), EMTRIVA® (emtricitabine), Epivir® or Epivir-HBV® (lamivudine), Epzicom® (abacavir sulfate/lamivudine), Trizivir® (abacavir sulfate/lamivudine/zidovudine), or VIREAD® (tenofovir disoproxil fumarate). These medicines have the same or similar active ingredients as TRUVADA
- Do not take TRUVADA with HEPSERA® for hepatitis B virus (HBV)

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Things to tell your healthcare provider

Tell your healthcare provider if you...

- **Are pregnant or plan to become pregnant.** There is an increased risk of HIV-1 infection during pregnancy. It is not known if TRUVADA can harm your unborn child. You and your healthcare provider will need to decide if TRUVADA is right for you. If you use TRUVADA while you are pregnant, talk to your healthcare provider about joining the TRUVADA Antiviral Pregnancy Registry
- **Are breast-feeding.** You should not breast-feed if you have HIV-1 because you may pass HIV-1 to your baby. Also, the components of TRUVADA (emtricitabine/tenofovir disoproxil fumarate) can pass into your breast milk, and it is not known if this will harm your baby. If you are a woman who has or will have a baby, talk with your healthcare provider about the best way to feed your baby
- **Have kidney problems or get kidney dialysis treatment**
- **Have bone problems**
- **Have liver problems, including hepatitis B virus infection**

Your healthcare provider needs to know what other medicines you take

- Make sure you tell your doctor if you take didanosine (VIDEX EC), atazanavir (REYATAZ), or lopinavir with ritonavir (KALETRA) because the doses of these medications may need to change

Tell your healthcare provider about all of the medicines you take. That means prescription and non-prescription medicines, vitamins, and herbal supplements. TRUVADA may affect the way other medicines work, and other medicines may affect how TRUVADA works.

Show a list of all your medicines to your healthcare provider or pharmacist when you get a new medicine.

Possible side effects of TRUVADA

TRUVADA may cause these serious side effects:

- **New or worse kidney problems,** including kidney failure. If you have had kidney problems in the past or need to take another medicine that can cause kidney problems, your healthcare provider may need to do blood tests to check your kidneys while you are taking TRUVADA
- **Bone problems.** Bone problems, like bone pain, softening, or thinning (which may lead to fractures), can occur. Your healthcare provider may need to do tests to check your bones
- **Changes in body fat.** These changes may include increased amount of fat in the upper back and neck (“buffalo hump”), breast, and around the main part of your body (trunk). Loss of fat from the legs, arms, and face may also happen. The cause and long-term health effects of these conditions are not known
- **Changes in your immune system (immune reconstitution syndrome).** This can occur if you have active HIV-1 infection and take TRUVADA

Complete management to lower the risk of acquiring HIV-1

Use TRUVADA for a PrEP indication only as part of a complete 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.

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Common side effects of TRUVADA

No new side effects emerged in the iPrEx and Partners PrEP clinical trials. The most common reported with the use of TRUVADA alone in these clinical trials include abdominal pain, headache, and decreased weight.

The most common side effects of EMTRIVA or VIREAD, the medicines in TRUVADA, when used with other anti–HIV-1 medicines are:

- Diarrhea
- Dizziness
- Nausea
- Headache
- Fatigue
- Abnormal dreams
- Problems sleeping
- Rash
- Depression
- Vomiting

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

Talk with your healthcare provider

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

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

Please see the Full Prescribing Information with Medication Guide, including **"What is the most important information I should know about TRUVADA?"** that goes with this brochure.

Make sure you understand the risks and benefits of taking TRUVADA for a PrEP indication as outlined in the TRUVADA Medication Guide and in the Agreement Form, and you have spoken with your healthcare provider about questions and concerns.

Notes

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GILEAD

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TRUVADA for a Pre-exposure Prophylaxis (PrEP) Indication

Training Guide for Healthcare Providers

Reference ID: 3159388

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

INDICATION

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

PRESCRIBING CONSIDERATIONS: When prescribing TRUVADA for pre-exposure prophylaxis:

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

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

BOXED WARNINGS: Use of TRUVADA for a PrEP Indication

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

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Why Use TRUVADA for a PrEP Indication?

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

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

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

Key Findings of the TRUVADA for a PrEP Indication Trials

The iPrEx Trial

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

The Partners PrEP Trial

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

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TRUVADA Safety Profile

IMPORTANT SAFETY INFORMATION

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

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

- **Comprehensive management to reduce the risk of acquiring HIV-1:** TRUVADA for a PrEP indication should only be used as part of a comprehensive prevention strategy that includes other prevention measures, such as safer sex practices, because TRUVADA is not always effective in preventing the acquisition of HIV-1
  - Counsel uninfected individuals at high risk about safer sex practices, including:
    - Using condoms consistently and correctly
    - Knowing their HIV-1 status and that of their partner(s)
    - Being tested for other sexually transmitted infections
    - Informing individuals about the importance of reducing sexually risky behaviors and supporting their efforts to do so
  - **Use TRUVADA to reduce the risk of acquiring HIV-1 only in individuals confirmed to be HIV-1 negative.** HIV resistance substitutions may emerge with individuals with undetected HIV-1 infection who are taking only TRUVADA because TRUVADA alone does not constitute a complete treatment regimen for HIV-1 infection. Therefore:
    - Confirm a negative HIV-1 test immediately prior to initiating TRUVADA for a PrEP indication. If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposures are suspected, delay starting PrEP for at least 1 month and reconfirm HIV-1 status or use a test approved by the FDA as an aid in the diagnosis of HIV-1 infection, including acute or primary HIV-1 infection
    - Screen for HIV-1 infection at least once every 3 months while taking TRUVADA for PrEP
    - Evaluate for signs or symptoms of acute HIV-1 infection prior to and while prescribing TRUVADA for a PrEP indication. If symptoms consistent with acute HIV-1 infection develop following a potential exposure event, PrEP should be discontinued until negative infection status is confirmed using a test approved by the FDA as an aid in the diagnosis of HIV-1, including acute or primary HIV-1 infection
  - Counsel all uninfected individuals to strictly adhere to their TRUVADA daily dosing schedule. The effectiveness of TRUVADA in reducing the risk of acquiring HIV-1 is strongly correlated with adherence and measurable drug levels
- **New onset or worsening renal impairment:** Can include acute renal failure and Fanconi syndrome. Assess creatinine clearance (CrCl) before prescribing TRUVADA. Monitor CrCl and serum phosphorus in individuals at risk for renal impairment. Avoid administering TRUVADA with concurrent or recent use of nephrotoxic drugs
  - **Do not prescribe TRUVADA for a PrEP indication for uninfected individuals with a creatinine clearance below 60 mL/min. If a decrease in CrCl is observed in uninfected individuals while using TRUVADA for PrEP, evaluate potential causes and re-assess potential risks and benefits of continued use**
- **HBV infection:** It is recommended that all individuals be tested for the presence of chronic hepatitis B virus (HBV) before initiating TRUVADA
  - HBV-uninfected individuals should be offered vaccination
- **Decreases in bone mineral density (BMD):** Consider assessment of BMD in individuals with a history of pathologic fracture or other risk factors for osteoporosis or bone loss
- **Redistribution/accumulation of body fat:** Observed in patients receiving antiretroviral therapy
- **Immune reconstitution syndrome:** May necessitate further evaluation and treatment in HIV-1–infected patients

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

- **Pregnancy:** There are no adequate and well-controlled trials in pregnant women. TRUVADA should be used during pregnancy only if clearly needed. If an uninfected individual becomes pregnant while taking TRUVADA for a PrEP indication, careful consideration should be given to whether use of TRUVADA should be continued, taking into account the potential increased risk of HIV-1 infection during pregnancy
  - A pregnancy registry is available. Enroll women taking TRUVADA for a PrEP indication by calling 1-800-258-4263
- **Nursing mothers:** Women infected with HIV-1 or taking TRUVADA for a PrEP indication should be instructed not to breast-feed. The components of TRUVADA (emtricitabine and tenofovir disoproxil fumarate) are excreted in breast milk, and it is not known if these can harm the infant
- **Pediatrics:** The TRUVADA for a PrEP indication is based on trials in adults

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

- Confirm a negative HIV-1 test immediately prior to initiating TRUVADA for a PrEP indication. If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposures are suspected, delay starting PrEP for at least 1 month and reconfirm HIV-1 status or use a test approved by the FDA as an aid in the diagnosis of HIV-1 infection, including acute or primary HIV-1 infection
- Screen for HIV-1 infection at least once every 3 months while taking TRUVADA for PrEP
- It is important to be alert to the signs of potential acute HIV-1 infection when prescribing TRUVADA for a PrEP indication. These include fever, headache, fatigue, arthralgia, vomiting, myalgia, diarrhea, pharyngitis, rash, night sweats, and cervical and inguinal adenopathy
- If symptoms consistent with acute HIV-1 infection develop following a potential exposure event, PrEP should be discontinued until negative infection status is confirmed using a test approved by the FDA as an aid in the diagnosis of HIV-1, including acute or primary HIV-1 infection
- HIV-1 resistance mutations may emerge in individuals with undetected HIV-1 infection who are taking TRUVADA for a PrEP indication

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

Important Safety Information

Drug Interactions

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

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

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Common Adverse Events

- In HIV-1–uninfected individuals in PrEP trials, adverse reactions that were reported by more than 2% of TRUVADA subjects and more frequently than by placebo subjects were headache, abdominal pain, and weight decreased
- The most common adverse events (incidence ≥10%) reported by HIV-1–infected subjects in clinical trials (in combination with efavirenz) are diarrhea, nausea, fatigue, headache, dizziness, depression, insomnia, abnormal dreams, and rash

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

Post-Training Review Questions

1. TRUVADA for a PrEP indication should be used only:

a. As part of a comprehensive HIV-1 prevention strategy that includes other preventive measures since TRUVADA is not always effective in preventing the acquisition of HIV-1

b. In individuals who have been counseled to strictly adhere to their TRUVADA daily dosing schedule since the effectiveness of TRUVADA in reducing the risk of acquiring HIV-1 is strongly correlated with adherence and measurable drug levels

c. In individuals who have a confirmed negative HIV-1 test prior to initiating and routinely while taking TRUVADA for a PrEP indication

d. All of the above

2. Which of the following statements is false?

a. TRUVADA should be used for a PrEP indication only in individuals confirmed to be HIV-1 negative

b. TRUVADA has been found to be safe and effective for pre-exposure prophylaxis to reduce the risk of acquiring HIV-1 through injection drug use

c. Women taking TRUVADA for a PrEP indication should not breast-feed their babies

d. TRUVADA for a PrEP indication is not always effective in preventing HIV-1

3. Which of the following items are not included on the Checklist for Prescribers for initiating TRUVADA for a PrEP indication?

a. Perform HBV screening test

b. Perform testing for TB

c. Confirm negative HIV-1 status of the individual

d. Confirm creatinine clearance is ≥60 mL/min

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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 PrEP of Sexually Acquired HIV-1 Infection provides which of the following information:

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

b. A confirmation that the prescriber has discussed the risks and benefits of using TRUVADA for a PrEP indication with the uninfected individual

c. A signature from the individual asserting that the prescriber has explained the risks and benefits of taking TRUVADA for a PrEP indication, including the need for adherence and a comprehensive prevention strategy, which includes safer sex practices

d. All of the above

Answer key: 1–d; 2-b; 3–b; 4–a; 5–c; 6–d; 7-d

Truvada®

200 mg emtri i i i i il fumarat 300 mg

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

GILEAD SCIENCES
565 SINCLAIR FRONTAGE RD
MILPITAS CA 95035-9905

BUSINESS REPLY MAIL
FIRST-CLASS MAIL PERMIT NO. 19 MILPITAS, CA

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UNITED STATES

((POCKET))

If you would like additional educational materials about TRUVADA for a PrEP indication, please select which ones you want and how many you would like us to send to you.

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

Your full name and degree: _____

Street address: _____

City: _____ State: _____ ZIP: _____

Your practice or clinic name: _____

Your specialty: _____

Telephone: _____ E-mail: _____

Terms and Conditions

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GILEAD

Truvada®
200 mg emtricitabine-tenofovir disoproxil fumarate 300 mg

Reference ID: 3159388 MOISTEN GLUE STRIP AND FOLD TO SEAL.

Notes

Truvada®
200 mg emtricitabine-tenofovir disoproxil fumarate 300 mg

Reference: TRUVADA [package insert]. Foster City, CA: Gilead Sciences, Inc; 2012.

Reference ID: 3159388

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

Healthcare Provider Training

Reference ID: 3159388

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

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

Reference ID: 3159388

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 was strongly correlated with adherence as demonstrated by measurable drug levels in a subgroup of clinical trials subjects
- 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 Warnings

- TRUVADA used for a PrEP indication must only be prescribed to individuals confirmed to be HIV-negative immediately prior to initiating and periodically (at least every 3 months) during use. Drug-resistant HIV-1 variants have been identified with the use of TRUVADA for a PrEP indication following undetected acute HIV-1 infection. Do not initiate TRUVADA for a PrEP indication if signs or symptoms of acute HIV infection are present unless negative infection status is confirmed

Boxed Warnings, cont.

- Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including VIREAD, a component of TRUVADA

- TRUVADA is not approved for the treatment of chronic hepatitis B virus (HBV) infection. Severe acute exacerbations of hepatitis B have been reported in patients coinfected with HBV and HIV-1 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 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

Reference ID: 3159388

Key Findings of the TRUVADA for a PrEP Indication Studies: The iPrEx Trial

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

Key Findings of the TRUVADA for a PrEP Indication Studies: The Partners PrEP Trial

- In another clinical study of TRUVADA for a PrEP indication, TRUVADA was shown to reduce HIV-1 acquisition by 75% in uninfected individuals in stable heterosexual serodiscordant relationships who also received comprehensive prevention services, including monthly HIV testing, evaluation of adherence, assessment of sexual behavior, and safety evaluations
- In a post-hoc case control study of plasma drug levels in about 10% of study subjects, risk reduction appeared to be the greatest in subjects with detectable plasma tenofovir. Efficacy was therefore strongly correlated with adherence. Risk reduction increased further in subjects with detectable plasma tenofovir

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

- Prescribe TRUVADA for PrEP only as part of a comprehensive prevention strategy that includes other prevention measures, such as safer sex practices, because TRUVADA 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 creatinine clearance (CrCl) before prescribing TRUVADA and as clinically appropriate during therapy
- Routinely monitor CrCl and serum phosphorus in individuals at risk of renal impairment
- Avoid administering TRUVADA with concurrent or recent use of nephrotoxic drugs
- Do not use TRUVADA for a PrEP indication in HIV-1 uninfected individuals with a CrCl below 60 mL/min
  - If a decrease in CrCl is observed in uninfected individuals while using TRUVADA for PrEP, evaluate potential causes and re-assess potential risks and benefits of continued use

Important Safety Information: Additional Warnings and Precautions

Decreases in bone mineral density (BMD)

- Consider assessment of BMD in individuals with a history of pathologic fracture or other risk factors for osteoporosis or bone loss

Redistribution/accumulation of body fat

- Observed in patients receiving antiretroviral therapy 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

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

Pregnancy

- TRUVADA has been evaluated in a limited number of women who are pregnant
- Physicians should assess risk benefit when considering TRUVADA for a PrEP indication in women who are pregnant and at increased risk of HIV-1 infection. Data suggest that there is a potential increased risk of HIV infection during pregnancy*
- 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
- 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

- Women infected with HIV-1 or taking TRUVADA for a PrEP indication should be instructed not to breast-feed. The components of TRUVADA are excreted in breast milk, and it is not known if these can harm the infant

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 negative
  - A negative HIV 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 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
  - It is important to be alert to the signs of potential acute HIV-1 infection when prescribing TRUVADA for a PrEP indication. These include fever, headache, fatigue, arthralgia, vomiting, myalgia, diarrhea, pharyngitis, rash, night sweats, and cervical and inguinal adenopathy
  - HIV-1 resistance mutations may emerge in individuals with undetected HIV-1 infection who are taking TRUVADA for a PrEP indication
    - Although TRUVADA is active against HIV-1, TRUVADA alone does not constitute a complete treatment regimen for HIV-1 infection
    - HIV-1–infected patients taking TRUVADA must take it with other antiretroviral agents to fully suppress virus replication and avoid the development of resistance

Important Safety Information: Drug Interactions and Common Adverse Events

Drug Interactions

- Coadministration with other products
  - Do not use TRUVADA with drugs containing emtricitabine or tenofovir disoproxil fumarate, or with drugs containing lamivudine. Do not administer in combination with HEPSERA® (adefovir dipivoxil)
  - 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

Agreement Form

for Initiating TRUVADA® for Pre-exposure Prophylaxis (PrEP) of Sexually Acquired HIV-1 Infection

Individual Label

Instructions: Review form with an uninfected individual who is about to start or is taking TRUVADA for a PrEP indication at each visit. File form in individual'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

Prescriber 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 uninfected individual about these risks, counsel the individual on risk reduction, monitor the individual appropriately, and report adverse events. Specifically, I attest to having done the following:

- Confirmed the negative HIV-1 status of this individual prior to starting TRUVADA for a PrEP indication
- Read the Full Prescribing Information
- Discussed with the uninfected individual the known safety risks with use
- 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 uninfected individual at high risk prior to prescribing TRUVADA for a PrEP indication
- Completed the items on the Checklist for Prescribers

Healthcare Provider Signature _____ Date _____

Uninfected Individual Agreement

By signing below, I acknowledge that I have been given an explanation of the risks and benefits of TRUVADA for a pre-exposure prophylaxis (PrEP) indication, and I understand them clearly. Specifically, I attest to the following:

- I have been given an explanation of and understand the importance of follow-up HIV-1 testing, and I agree to have repeat HIV-1 screening tests as scheduled by my healthcare provider
- I have been given an explanation of and understand the safety risks involved with using TRUVADA for PrEP
- I have been given an explanation of and understand the importance of following 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

Uninfected Individual Signature _____ Date _____

Truvada® 200 mg emtricitabine 300 mg tenofovir disoproxil fumarate

GILEAD

Reference ID: 3159388

Checklist for Prescribers:

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

Individual Label

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:

- ☐ 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)
- ☐ 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 PrEP to confirm HIV-1 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
- ☐ Performed HBV screening test. Offered HBV vaccination as appropriate
- ☐ Confirmed creatinine clearance (CrCl) ≥60 mL/min. If a decrease in CrCl is observed in uninfected individuals while using TRUVADA for PrEP, evaluate potential causes and re-assess potential risks and benefits of continued use
- ☐ Confirmed that the uninfected individual at high risk is not taking other HIV-1 medications or hepatitis B medications
- ☐ Provided education on where information about PrEP can be accessed
- ☐ Discussed potential adverse events and side effects
- ☐ Reviewed the TRUVADA Medication Guide with the uninfected individual at high risk
- ☐ Evaluated risk/benefit for women who may be pregnant or may want to become pregnant

Truvada® 200 mg emtricitabine 300 mg tenofovir disoproxil fumarate

GILEAD

Reference ID: 3159388

TRU... Prophylaxis (PrEP) Indication

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 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 and important prescribing considerations**

Review the online training for prescribers →

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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.

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.

Access REMS resources →

Important Safety Information About TRUVADA for a PrEP Indication

BOXED WARNINGS:

- **TRUVADA for a PrEP indication must only be prescribed to individuals confirmed to be HIV-1 negative**

TRUVADA for a Pre-exposure Prophylaxis (PrEP) Indication

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 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 and important prescribing considerations**

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REMS Information

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Important Safety Information About TRUVADA for a PrEP Indication

BOXED WARNINGS:

- **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 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 coinfected 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 HBV-infected patients who discontinue TRUVADA. If appropriate, initiation of anti-hepatitis B therapy may be warranted**

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.

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

- **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, mylagia, 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 as demonstrated by measurable drug levels in clinical trials
- **New or worsening renal impairment:** Acute renal impairment including Fanconi syndrome may occur. Assess creatinine clearance (CrCl) before initiating therapy. Routine monitoring of CrCl and serum phosphorus is recommended for patients at risk for renal impairment. Avoid administering TRUVADA with concurrent or recent use of nephrotoxic drugs
  - **Do not prescribe TRUVADA for uninfected individuals with a creatinine clearance below 60 mL/min.** If a decrease in CrCl is observed in uninfected individuals while using TRUVADA for PrEP, evaluate potential causes and re-assess potential risks and benefits of continued use
- **HBV Infection:** It is recommended that all individuals be tested for the presence of chronic hepatitis B virus (HBV) before initiating TRUVADA. HBV-uninfected individuals should be offered vaccination
- **Decreases in bone mineral density may occur.** Consider assessing in individuals with history of bone fractures, osteoporosis, or bone loss
- **Redistribution/accumulation of body fat:** observed in patients receiving antiretroviral therapy
- **Immune reconstitution syndrome:** has been reported in HIV-1 infected patients treated with combination antiretroviral therapy, including TRUVADA. Autoimmune disorders my occur in the setting of immune reconstitution
- **Coadministration with other products:** Do not co-administer with other drugs containing emtricitabine or tenofovir disoproxil fumarate or lamivudine. Do not administer in combination with HEPSERA® (adefovir dipivoxil)

Common Adverse Reactions

Most common adverse reactions (incidence ≥10%) (in combination with efavirenz) are diarrhea, nausea, fatigue, headache, dizziness, depression, insomnia, abnormal dreams, and rash. No new adverse reactions were reported in clinical trials of TRUVADA for PrEP. 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.

Potential drug interactions: Caution should be exercised when administering TRUVADA with didanosine, atazanavir and lopinavir/ritonavir due to the potential for toxicities.

Please see **Full Prescribing Information** for more information about potential drug interactions.

Use of TRUVADA for PrEP in Specific Populations

- **Pregnancy:** There are no adequate and well-controlled trials in pregnant women. TRUVADA should be used during pregnancy only if clearly needed. If an uninfected individual becomes pregnant while taking TRUVADA for a PrEP indication, careful consideration should be given to whether use of TRUVADA should be continued, taking into account the potential increased risk of HIV-1 infection during pregnancy
  - A pregnancy registry is available. Enroll women taking TRUVADA for a PrEP indication by calling 1-800-258-4263
- **Nursing mothers:** Women infected with HIV-1 or taking TRUVADA for a PrEP indication should be instructed not to breast-feed. The components of TRUVADA (emtricitabine and tenofovir disoproxil fumarate) are excreted in breast milk and the risk to the infant is not known
- **Pediatrics:** The TRUVADA for a PrEP indication is based on studies in adults

Dosage and Administration

- Adults: Dosage of TRUVADA for PrEP for adults is one tablet once per day orally with or without food
- Dose Adjustment for Renal Impairment: **None. Do not prescribe TRUVADA for unifected individuals with CrCL below 60 mL/min.** If a decrease in CrCl is observed in uninfected individuals while using TRUVADA for PrEP, evaluate potential causes and re-assess potential risks and benefits of continued use

Indication and Usage for Pre-exposure Prophylaxis

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.

Factors that may help identify individuals at high risk include: 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.

The following points must be considered when prescribing TRUVADA for pre-exposure prophylaxis:

- 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 was strongly correlated with adherence and measurable drug levels in clinical trials
- Confirm a negative HIV-1 test immediately prior to initiating TRUVADA for a PrEP indication. If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposures are suspected, delay starting PrEP for at least 1 month and reconfirm HIV-1 status or use a test approved by the FDA as an aid in the diagnosis of HIV-1 infection, including acute or primary HIV-1 infection
- Screen for HIV-1 infection at least once every 3 months while taking TRUVADA for PrEP
- Do not initiate TRUVADA for a PrEP indication if signs or symptoms of acute HIV-1 infection are present

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.

Truvada

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

Healthcare Provider Training

NEXT

Prophylaxis (PrEP) Indication

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 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 and important prescribing considerations**

Review the online training for prescribers →

EMS Information

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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.

Access REMS resources →

Important Safety Information About TRUVADA for a PrEP Indication

BOXED WARNINGS:

- **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 in combination with other antiretrovirals**

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Indication

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- 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

Prophylaxis (PrEP) Indication

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Access REMS resources →

Important Safety Information About TRUVADA for a PrEP Indication

BOXED WARNINGS:

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Factors to Help Identify Individuals at High Risk

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- Has 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, 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

identify individuals at high risk for sexually acquired HIV-1 and important prescribing considerations

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Risk Evaluation and Mitigation Strategy EMS) is a strategy to manage known or ential serious risks associated with a drug duct and is required by the Food and Drug ministration (FDA) to ensure that the benefits he drug outweigh its risks.

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.

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Important Safety Information About TRUVADA for a PrEP Indication

BOXED WARNINGS:

- **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 in combination with other antiretrovirals**

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When Prescribing TRUVADA for a PrEP Indication, Healthcare Providers MUST:

PREV NEXT

- 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 was strongly correlated with adherence as demonstrated by measurable drug levels in a subgroup of clinical trials subjects
- 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 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 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

EMS Information

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BOXED WARNINGS:

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- **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

Boxed Warnings

- TRUVADA used for a PrEP indication must only be prescribed to individuals confirmed to be HIV-negative immediately prior to initiating and periodically (at least every 3 months) during use. Drug-resistant HIV-1 variants have been identified with the use of TRUVADA for a PrEP indication following undetected acute HIV-1 infection. Do not initiate TRUVADA for a PrEP indication if signs or symptoms of acute HIV infection are present unless negative infection status is confirmed

PREV NEXT

TRUVADA for a PrEP indication—in combination with safer sex practices—can help reduce the risk of sexually acquired HIV-1 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 and important prescribing considerations**

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Important Safety Information About TRUVADA for a PrEP Indication

BOXED WARNINGS:

- **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**
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Boxed Warnings (Continued)

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- Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including VIREAD, a component of TRUVADA
- TRUVADA is not approved for the treatment of chronic hepatitis B virus (HBV) infection. Severe acute exacerbations of hepatitis B have been reported in patients coinfected with HBV and HIV-1 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

identify individuals at high risk for sexually acquired HIV-1 and important prescribing considerations

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Important Safety Information About TRUVADA for a PrEP Indication

BOXED WARNINGS:

- **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 in combination with other antiretrovirals**

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Why Use TRUVADA for a PrEP Indication?

PREV NEXT

- 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 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

EMS Information

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Important Safety Information About TRUVADA for a PrEP Indication

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- **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**

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Key Findings of the TRUVADA for a PrEP Indication Studies: The iPrEx Trial

PREV NEXT

- 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

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- **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**

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Key Findings of the TRUVADA for a PrEP Indication Studies: The Partners PrEP Trial

PREV NEXT

- 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

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EMS Information

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- **Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use**

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

NEXT

- 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

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Truvada

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PREV

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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 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

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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 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
  - 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

EMS Information

Risk Evaluation and Mitigation Strategy
EMS) is a strategy to manage known or
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REMS program to educate and inform
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Access REMS resources →

Important Safety Information About TRUVADA for a PrEP Indication

BOXED WARNINGS:

- **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 in combination with other antiretrovirals**

Truvada

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PREV

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

NEXT

- 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

practices—can help reduce the risk of sexually acquired HIV-1 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 and important prescribing considerations**

Review the online training for prescribers →

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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.

Access REMS resources →

Important Safety Information About TRUVADA for a PrEP Indication

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- **Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use**

Truvada

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Important Safety Information: Additional Warnings and Precautions

New Onset or Worsening Renal Impairment

- Can include acute renal failure and Fanconi syndrome
- Assess creatinine clearance (CrCl) before prescribing TRUVADA and as clinically appropriate during therapy
- Routinely monitor CrCl and serum phosphorus in individuals at risk of renal impairment
- Avoid administering TRUVADA with concurrent or recent use of nephrotoxic drugs
- Do not use TRUVADA for a PrEP indication in HIV-1 uninfected individuals with a CrCl below 60 mL/min
  - If a decrease in CrCl is observed in uninfected individuals while using TRUVADA for PrEP, evaluate potential causes and re-assess potential risks and benefits of continued use

Review the online training for prescribers →

EMS Information

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Access REMS resources →

Important Safety Information About TRUVADA for a PrEP Indication

BOXED WARNINGS:

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Truvada

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Important Safety Information: Additional Warnings and Precautions

PREV NEXT

Decreases in bone mineral density (BMD)

- Consider assessment of BMD in individuals with a history of pathologic fracture or other risk factors for osteoporosis or bone loss

Redistribution/accumulation of body fat

- Observed in patients receiving antiretroviral therapy 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

Review the online training for prescribers →

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Access REMS resources →

Important Safety Information About TRUVADA for a PrEP Indication

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

Pregnancy

- TRUVADA has been evaluated in a limited number of women who are pregnant
- Physicians should assess risk benefit when considering TRUVADA for a PrEP indication in women who are pregnant and at increased risk of HIV-1 infection. Data suggest that there is a potential increased risk of HIV infection during pregnancy*
- 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
- 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.

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Important Safety Information About TRUVADA for a PrEP Indication

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- **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**

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

Nursing Mothers

- Women infected with HIV-1 or taking TRUVADA for a PrEP indication should be instructed not to breast-feed. The components of TRUVADA are excreted in breast milk, and it is not known if these can harm the infant

Pediatrics

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

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 and important prescribing considerations**

Review the online training for prescribers →

EMS Information

Risk Evaluation and Mitigation Strategy EMS) is a strategy to manage known or ential serious risks associated with a drug duct and is required by the Food and Drug ministration (FDA) to ensure that the benefits he drug outweigh its risks.

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.

Access REMS resources →

Important Safety Information About TRUVADA for a PrEP Indication

BOXED WARNINGS:

- **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**
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PREV

NEXT

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 negative
  - A negative HIV 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 negative
  - 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
    - 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

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cess REMS resources →

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200 mg

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Important Safety Information: Drug Interactions and Common Adverse Events

Drug Interactions

- Coadministration with other products
  - Do not use TRUVADA with drugs containing emtricitabine or tenofovir disoproxil fumarate, or with drugs containing lamivudine. Do not administer in combination with HEPSERA® (adefovir dipivoxil)
  - For further details about TRUVADA drug interactions, please see the Full Prescribing Information for TRUVADA

Common Adverse Reactions

- 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

Review the online training for prescribers →

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Access REMS resources →

Important Safety Information About TRUVADA for a PrEP Indication

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Truvada

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Additional Educational Materials

PREV

NEXT

- 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

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Important Safety Information About TRUVADA for a PrEP Indication

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- **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**

Prophylaxis (PrEP) Indication

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 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 and important prescribing considerations**

Review the online training for prescribers →

EMS Information

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.

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.

Access REMS resources →

Important Safety Information About TRUVADA for a PrEP Indication

BOXED WARNINGS:

- **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**
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EMS Information

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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.

Access REMS resources →

Important Safety Information About TRUVADA for a PrEP Indication

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To help Gilead and the FDA understand who has viewed this training, please tell us the following

PREV NEXT

Your Specialty:

Indicate your specialty

- Indicate your specialty
- Internal medicine
- Family practice
- General medicine
- Infectious diseases
- Obstetrics/gynecology
- Addiction medicine
- Other

Your Profession:

Select your profession

- Select your profession
- MD
- PA
- RN
- Other

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Access REMS resources →

Important Safety Information About TRUVADA for a PrEP Indication

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Thank you

PREV Close

TRUVADA for a Pre-exposure Prophylaxis (PrEP) Indication

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 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 and important prescribing considerations**

Review the online training for prescribers →

REMS Information

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.

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.

Access REMS resources →

Important Safety Information About TRUVADA for a PrEP Indication

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- **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**

About TRUVADA for a PrEP Indication

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

When prescribing TRUVADA for pre-exposure prophylaxis, 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 TRUVADA daily dosing schedule because the effectiveness of TRUVADA in reducing the risk of acquiring HIV-1 was strongly correlated with adherence as demonstrated by measurable drug levels in clinical trials
- 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

Mechanism of action for pre-exposure prophylaxis

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: Comprehensive Management →

REMS Center

Materials

Download important materials for healthcare providers and uninfected individuals about TRUVADA for a PrEP indication →

Post-Training Review Questions

Assess your knowledge of TRUVADA for a PrEP indication by answering a series of review questions →

Comprehensive Management

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.

- 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

Prescribe TRUVADA to reduce the risk of acquiring HIV-1 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.

- 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 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. 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 uninfected individuals to strictly adhere to the recommended TRUVADA daily 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 clinical trials.

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.

Access tools that can help you manage and counsel individuals on the correct and safe use of TRUVADA for a PrEP indication.

Checklist for Prescribers →

Agreement Form →

Next: Important Safety Information →

REMS Center

Materials

Download important materials for healthcare providers and uninfected individuals about TRUVADA for a PrEP indication →

Post-Training Review Questions

Assess your knowledge of TRUVADA for a PrEP indication by answering a series of review questions →

Important Safety Information

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:

Boxed WARNINGS | Adverse Reactions | Drug Interactions | Warnings & Precautions | Specific Populations | Indication

Important Safety Information About TRUVADA for a PrEP Indication

BOXED WARNINGS:

- **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 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 coinfected 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 HBV-infected patients who discontinue TRUVADA. If appropriate, initiation of anti-hepatitis B therapy may be warranted**

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.

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

- **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, mylagia, 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 as demonstrated by measurable drug levels in clinical trials
- **New or worsening renal impairment:** Acute renal impairment including Fanconi syndrome may occur. Assess creatinine clearance (CrCl) before initiating therapy. Routine monitoring of CrCl and serum phosphorus is recommended for patients at risk for renal impairment. Avoid administering TRUVADA with concurrent or recent use of nephrotoxic drugs
  - **Do not prescribe TRUVADA for uninfected individuals with a creatinine clearance below 60 mL/min.** If a decrease in CrCl is observed in uninfected individuals while using TRUVADA for PrEP, evaluate potential causes and re-assess potential risks and benefits of continued use
- **HBV Infection:** It is recommended that all individuals be tested for the presence of chronic hepatitis B virus (HBV) before initiating TRUVADA. HBV-uninfected individuals should be offered vaccination
- **Decreases in bone mineral density may occur.** Consider assessing in individuals with history of bone fractures, osteoporosis, or bone loss
- **Redistribution/accumulation of body fat:** observed in patients receiving antiretroviral therapy
- **Immune reconstitution syndrome:** has been reported in HIV-1 infected patients treated with combination antiretroviral therapy, including TRUVADA. Autoimmune disorders my occur in the setting of immune reconstitution
- **Coadministration with other products:** Do not co-administer with other drugs containing emtricitabine or tenofovir disoproxil fumarate or lamivudine. Do not administer in combination with HEPSERA® (adefovir dipivoxil)

Common Adverse Reactions

Most common adverse reactions (incidence ≥10%) (in combination with efavirenz) are diarrhea, nausea, fatigue, headache, dizziness, depression, insomnia, abnormal dreams, and rash. No new adverse reactions were reported in clinical trials of TRUVADA for PrEP. 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.

Potential drug interactions: Caution should be exercised when administering TRUVADA with didanosine, atazanavir and lopinavir/ritonavir due to the potential for toxicities.

Please see Full Prescribing Information for more information about potential drug interactions.

Use of TRUVADA for PrEP in Specific Populations

- **Pregnancy:** There are no adequate and well-controlled trials in pregnant women. TRUVADA should be used during pregnancy only if clearly needed. If an uninfected individual becomes pregnant while taking TRUVADA for a PrEP indication, careful consideration should be given to whether use of TRUVADA should be continued, taking into account the potential increased risk of HIV-1 infection during pregnancy
  - A pregnancy registry is available. Enroll women taking TRUVADA for a PrEP indication by calling 1-800-258-4263
- **Nursing mothers:** Women infected with HIV-1 or taking TRUVADA for a PrEP indication should be instructed not to breast-feed. The components of TRUVADA (emtricitabine and tenofovir disoproxil fumarate) are excreted in breast milk and the risk to the infant is not known
- **Pediatrics:** The TRUVADA for a PrEP indication is based on studies in adults

Dosage and Administration

- Adults: Dosage of TRUVADA for PrEP for adults is one tablet once per day orally with or without food
- Dose Adjustment for Renal Impairment: **None. Do not prescribe TRUVADA for unifected individuals with CrCL below 60 mL/min.** If a decrease in CrCl is observed in uninfected individuals while using TRUVADA for PrEP, evaluate potential causes and re-assess potential risks and benefits of continued use

Indication and Usage for Pre-exposure Prophylaxis

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.

Factors that may help identify individuals at high risk include: 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.

The following points must be considered when prescribing TRUVADA for pre-exposure prophylaxis:

- 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 was strongly correlated with adherence and measurable drug levels in clinical trials
- Confirm a negative HIV-1 test immediately prior to initiating TRUVADA for a PrEP indication. If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposures are suspected, delay starting PrEP for at least 1 month and reconfirm HIV-1 status or use a test approved by the FDA as an aid in the diagnosis of HIV-1 infection, including acute or primary HIV-1 infection
- Screen for HIV-1 infection at least once every 3 months while taking TRUVADA for PrEP
- Do not initiate TRUVADA for a PrEP indication if signs or symptoms of acute HIV-1 infection are present

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.

Next: Checklist For Prescribers →

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Checklist for Prescribers

Before prescribing TRUVADA for a PrEP indication, it's important that you complete the **Checklist for Prescribers** with uninfected individuals and file in the individual's medical record. On each visit with an uninfected individual, complete the following steps:

- Complete high risk evaluation of uninfected individual
- 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) 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 confirm 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
- Perform HBV screening test. Offer HBV vaccination as appropriate
- Confirm creatinine clearance (CrCl) ≥60 mL/min. If a decrease in CrCl is observed in uninfected individuals while using TRUVADA for PrEP, evaluate potential causes and re-assess potential risks and benefits of continued use
- 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 PrEP can be accessed
- Discuss potential adverse events and side effects
- Review the **TRUVADA Medication Guide** with the uninfected individual at high risk
- Evaluate risk/benefit for women who may be pregnant or may want to become pregnant

Next: Agreement Form →

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Agreement Form

As part of helping uninfected individuals understand the commitment in taking TRUVADA for a PrEP indication, the Agreement Form for Initiating TRUVADA for PrEP of Sexually Acquired HIV-1 Infection 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:

- 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

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.**

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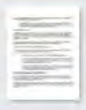
On this page, you'll find downloadable resources for you and uninfected individuals. You will need Adobe Acrobat installed on your computer to view these resources. If you do not have it and would like to download it, please click here.

DEAR HEALTHCARE PROVIDER LETTER



Information for healthcare providers on the new TRUVADA indication for pre-exposure prophylaxis (PrEP)

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TRAINING GUIDE FOR HEALTHCARE PROVIDERS

A comprehensive overview of TRUVADA for a PrEP indication

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IMPORTANT SAFETY INFORMATION FOR HEALTHCARE PROVIDERS

Important safety information about TRUVADA for a PrEP indication

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SAFETY INFORMATION FACT SHEET

A detailed overview of the safety information for TRUVADA for a PrEP indication

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AGREEMENT FORM FOR INITIATING TRUVADA FOR PrEP OF SEXUALLY ACQUIRED HIV-1 INFECTION

Form that should be reviewed with an individual considering/taking TRUVADA for a PrEP indication

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CHECKLIST FOR PRESCRIBERS

Tool for facilitating appropriate prescribing of TRUVADA for a PrEP indication

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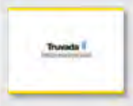
MEDICATION GUIDE



A comprehensive guide for uninfected individuals getting started on TRUVADA for a PrEP indication

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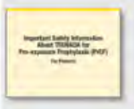
IMPORTANT SAFETY INFORMATION FOR UNINFECTED INDIVIDUALS



An easy-to-understand guide on the most important safety information about TRUVADA for a PrEP indication

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FULL PRESCRIBING INFORMATION

Full prescribing information for TRUVADA for a PrEP indication

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Post-Training Review Questions

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.

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(function () { TP.initializeAssessment(); })();

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
- In individuals who have been counseled to strictly adhere to their TRUVADA daily dosing schedule, since the effectiveness of TRUVADA in reducing the risk of acquiring HIV-1 is strongly correlated with adherence and measurable drug levels
- 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

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x

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 through injection drug use
- Women taking TRUVADA for a PrEP indication should not breast-feed their babies
- TRUVADA for a PrEP indication is not always effective in preventing HIV-1

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Which of the following items are not included on the Checklist for Prescribers for initiating TRUVADA for a PrEP indication?

- 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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x

Hepatic function should be monitored closely in:

- HBV-infected individuals who discontinue TRUVADA
- All people taking TRUVADA
- All people who discontinue TRUVADA
- None of the above

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In clinical trials evaluating TRUVADA for a PrEP indication, which of the following adverse reactions was not common?

- Abdominal pain
- Headache
- Dizziness
- Decreased weight

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x

TRUVADA for a PrEP indication is indicated only for:

- Men who are at high risk for sexually acquired HIV-1 infection
- Adults who are at high risk of acquiring HIV-1 infection by any means
- Adults who are at high risk of acquiring HIV-1 infection through injection drug use
- Adults who are at high risk for sexually acquired HIV-1 infection

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x

The Agreement Form for Initiating TRUVADA for PrEP of Sexually Acquired HIV-1 Infection provides which of the following information:

- A list of activities that put individuals at risk for sexually acquired HIV-1
- A confirmation that the prescriber has discussed the risks and benefits of using TRUVADA for a PrEP indication with the uninfected individual
- 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
- All of the above

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Site Map

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

/s/

DEBRA B BIRNKRANT
07/16/2012