

Prior Authorization DRUG Guidelines

TRUVADA (Tenofovir and emtricitabine)

Effective Date: 1/28/14

Date Developed: 1/28/14 by Catherine Sanders, MD

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Truvada is a combination Antiretroviral Agent, Reverse Transcriptase Inhibitor (Nucleoside) and Reverse Transcriptase Inhibitor (Nucleotide) used in the treatment of HIV-1 infections. Emtricitabine is a cytosine analogue while tenofovir disoproxil fumarate (TDF) is an analog of adenosine 5'-monophosphate. Each drug interferes with HIV viral RNA dependent DNA polymerase resulting in inhibition of viral replication.

Pre-Authorization Criteria:

Truvada is used to treat HIV-1 infection in combination with other antiretroviral agents in adults and pediatric patient greater than or equal to 12 years of age. It is recommended as a component of preferred regimens (in combination with atazanavir/ritonavir or darunavir/ritonavir or efavirenz or raltegravir) in antiretroviral-naïve patients

Truvada will also be approved for use in pre-exposure prophylaxis (PrEP) for prevention of HIV-1 infection in adults who are at high risk for acquiring HIV. High risk includes those with partners known to be HIV-1 infected or who engage 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
- Use of illicit drugs or alcohol dependence
- Incarceration
- Partner of unknown HIV-1 status with any of the above risk factors

When prescribing PrEP healthcare providers MUST:

- Include PrEP as part of a comprehensive prevention strategy because PrEP alone is not always effective in preventing HIV-1 infection
 - Counsel all uninfected patients to strictly adhere to the dosing schedule, because adherence was strongly correlated with effectiveness in clinical trials
 - Confirm a negative HIV-1 test prior to starting PrEP; if a candidate has acute viral infection symptoms and unprotected exposure events <1 month prior, delay PrEP for at least 1 month and retest HIV-1 status or use a Food and Drug Administration (FDA) test approved for HIV-1 diagnosis, including acute or primary HIV-1 infection
 - Retest for HIV-1 infection at least every 3 months while the patient receives PrEP
 - Confirmation that creatinine clearance value ≥ 60 mL/min before initiating Truvada for PrEP
- AND

- Serum creatinine and calculate creatinine clearance checks performed at 3 months after initiation and then every 6 months thereafter.

Truvada is not recommended as a component of a triple nucleoside regimen due to potential for early virological failure. Clinical trials in HIV-infected patients whose regimens contained only three nucleoside reverse transcriptase inhibitors (NRTI) show less efficacy, early virologic failure and high rates of resistance substitutions. Triple drug regimens with two NRTIs in combination with a non-nucleoside reverse transcriptase inhibitor or a HIV-1 protease inhibitor are usually more effective.

The following are unlabeled uses of Truvada and are therefore not covered:

- Treatment of hepatitis B in patients with antiviral-resistant HBV or coinfection with HIV
- Pre-exposure prophylaxis (PrEP) for prevention of HIV-1 infection in injecting drug users (IDU) who are at risk for parenteral acquisition of HIV but not at risk for sexual acquisition of HIV
- Postexposure prophylaxis (PEP) for occupational exposure to HIV

VCHCP requires that Truvada be prescribed by an Immunology Clinic physician with current American Academy of HIV Medicine (AAHIVM) certification or a physician boarded in Infectious Disease; except for PrEP and PEP. Primary Care Physicians (PCP) can prescribe PrEP and PEP. Note: Recommended as first-line therapy for PEP in combination with raltegravir (Isentress) in antiretroviral naive patients.

In addition, Truvada is included in the REMS (Risk Evaluation and Mitigation Strategies) program and there are specific prescriber requirements, which include the following:

Prescribers are encouraged to participate in the emtricitabine/tenofovir disoproxil fumarate for a PrEP Indication Healthcare Provider Education Program (See Attachment 3), and use the Agreement Form (See attachment 1) and Checklist for Initiating Emtricitabine/Tenofovir Disoproxil Fumarate for Pre-Exposure Prophylaxis (PrEP) (See attachment 2) to counsel patients receiving PrEP at each office visit. More training materials and forms can be accessed at

<https://www.accessdata.fda.gov/scripts/cder/remis/index.cfm?event=RemisDetails.page&REMS=365>

VCHCP requires that at a minimum, providers should participate in the Risk Evaluation and Mitigation Strategies (REMS) program. Registered providers can be found under Find a PrEP provider:

<https://www.pleaseprepmo.org/>

The Plan requires that the Agreement Form (Attachment 1) and Checklist for Providers Initiating the Medication (Attachment 2) are submitted with the medical records when requesting prior authorization for Truvada.

Medication Guide:

An FDA-approved patient medication guide, which is available with the product information and at <http://www.fda.gov/downloads/Drugs/DrugSafety/UCM312307.pdf>, must be dispensed with this medication.

Dosing: Adult:

Note: Avoid concurrent use with adefovir or lamivudine-containing products or other emtricitabine- and/or tenofovir-containing products.

HIV-1 infection: Oral: One tablet (emtricitabine 200 mg and tenofovir 300 mg) once daily. Note:

Recommended as a component of preferred regimens (in combination with atazanavir/ritonavir or darunavir/ritonavir or efavirenz or raltegravir) in antiretroviral-naïve patients (DHHS, 2013).

Preexposure prophylaxis (PrEP) for prevention of HIV infection in uninfected high-risk individuals: Oral: One tablet (emtricitabine 200 mg and tenofovir 300 mg) once daily

Hepatitis B treatment in patients with antiviral-resistant HBV or coinfection with HIV (unlabeled use): Oral: One tablet (emtricitabine 200 mg and tenofovir 300 mg) once daily (Lok, 2009)

Occupational HIV postexposure, prophylaxis (PEP) (unlabeled use): Oral: One tablet (emtricitabine 200 mg and tenofovir 300 mg) once daily for 4 weeks with concomitant raltegravir. Recommended as preferred therapy (Kuhar, 2013)

PrEP for prevention of HIV infection in injecting drug users (IDU) who are at risk for parenteral acquisition of HIV but not at risk for sexual acquisition of HIV (unlabeled use): Oral: One tablet (emtricitabine 200 mg and tenofovir 300 mg) once daily (CDC, 2013)

Dosing: Pediatric:

Note: Avoid concurrent use with adefovir or lamivudine-containing products or other emtricitabine- and/or tenofovir-containing products.

HIV-1 infection: Children ≥ 12 years (≥ 35 kg) and Adolescents (≥ 35 kg): Oral: One tablet (emtricitabine 200 mg and tenofovir 300 mg) once daily. Note: Recommended as a component of preferred regimens (in combination with atazanavir/ritonavir or darunavir/ritonavir or efavirenz or raltegravir) in antiretroviral-naïve patients (DHHS, 2013).

Dosing: Geriatric:

Refer to adult dosing.

Dosing: Renal Impairment:

HIV-1 infection: Adults:

$Cl_{cr} \geq 50$ mL/minute: No dosage adjustment necessary

Cl_{cr} 30-49 mL/minute: Increase interval to every 48 hours.

$Cl_{cr} < 30$ mL/minute or hemodialysis: Not recommended.

PrEP: Adults:

$Cl_{cr} \geq 60$ mL/minute: No dosage adjustment necessary

$Cl_{cr} < 60$ mL/minute: Not recommended.

Dosing: Hepatic Impairment:

No dosing adjustment necessary for tenofovir in moderate-to-severe hepatic compromise; no specific data available on emtricitabine in hepatic impairment, but given limited hepatic metabolism, dose adjustments are unlikely.

Dosage Forms: U.S.:

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Tablet:

Truvada: Emtricitabine 200 mg and tenofovir disoproxil fumarate 300 mg

Generic Equivalent Available: U.S.-No

Exceptions:

Truvada is not for use for preexposure prophylaxis (PrEP) in patients with unknown or HIV-1 positive status.

Truvada is not covered for the following unlabeled uses: Treatment of hepatitis B in patients with antiviral-resistant HBV or coinfection with HIV; pre-exposure prophylaxis (PrEP) for prevention of HIV-1 infection in injecting drug users (IDU) who are at risk for parenteral acquisition of HIV but not at risk for sexual acquisition of HIV; postexposure prophylaxis (PEP) for occupational exposure to HIV

Truvada is not for use in patients treated for HIV-1 infection with creatinine clearance <30 mL/minute or patients treated for pre-exposure prophylaxis with creatinine clearance <60 mL/minute as dosage adjustment is not possible with fixed-dose.

Adverse Reactions:

See individual agents.

Other Severe Less Common Reactions: lactic acidosis, hepatomegaly, hepatotoxicity, HBV exacerbation post-treatment, nephrotoxicity, rhabdomyolysis, myopathy, osteomalacia, fractures, pancreatitis, neutropenia, anemia, immune reconstitution syndrome, autoimmune disorders, fat redistribution, hypersensitivity reactions,

U.S. BOXED WARNING:

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, associated with nucleoside analogue use alone or in combination; suspend treatment if clinical or laboratory findings suggest lactic acidosis or hepatotoxicity

Safety and efficacy not established in HIV/HBV co-infection; severe acute HBV exacerbations in HBV/HIV co-infected pts with discontinuation of emtricitabine or tenofovir; monitor hepatic function closely for at least several months in HBV/HIV co-infected pts who discontinue emtricitabine/tenofovir; initiate anti-HBV treatment if needed

Only prescribe for pre-exposure prophylaxis use in HIV-negative pts; confirm HIV status immediately before treatment, then every 3months; drug-resistant HIV variants identified with use following undetected acute HIV infection; do not start in pts with acute HIV infection signs and symptoms unless HIV-negative status confirmed

References:

1. Baeten JM, Donnell D, Ndase P, et al, "Antiretroviral Prophylaxis for HIV Prevention in Heterosexual Men and Women," *N Engl J Med*, 2012, 367(5):399-410. [PubMed [22784037](#)]
2. Centers for Disease Control and Prevention (CDC), "Interim Guidance: Preexposure Prophylaxis for the Prevention of HIV infection in Men Who Have Sex with Men". *MMWR Morb Mortal Wkly Rep*, 2011, 60(3):65-8. [PubMed [21270743](#)]

3. Centers for Disease Control and Prevention (CDC), "Interim Guidance for Clinicians Considering the Use of Preexposure Prophylaxis for the Prevention of HIV Infection in Heterosexually Active Adults," *MMWR Morb Mortal Wkly Rep*, 2012, 61(31):586-9. [PubMed [22874836](#)]
4. Centers for Disease Control and Prevention (CDC), "Interim Guidance: Preexposure Prophylaxis for the Prevention of HIV Infection: PrEP for Injecting Drug Users," *MMWR Morb Mortal Wkly Rep*, 2013, 62(23):463-5. [PubMed [23760186](#)]
5. DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents, "Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents, Department of Health and Human Services," February 12, 2013;1-267. Available at <http://www.aidsinfo.nih.gov>
6. Grant RM, Lama JR, Anderson PL, et al, "Pre-exposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex With Men", *N Engl J Med*, 2010, 363(27):2587-99. [PubMed [21091279](#)]
7. Kuhar DT, Henderson DK, Struble KA, et al, "Updated US Public Health Service Guidelines for the Management of Occupational Exposures to Human Immunodeficiency Virus and Recommendations for Postexposure Prophylaxis," *Infect Control Hosp Epidemiol*, 2013, 34(9): 875-92. [PubMed [23917901](#)]
8. Lok AS and McMahon BJ, "Chronic Hepatitis B," *Hepatology*, 2007, 45(2):507- 39. [PubMed [17256718](#)]
9. Thigpen MC, Kebaabetswe PM, Paxton LA, et al, "Antiretroviral Preexposure Prophylaxis for Heterosexual HIV Transmission in Botswana," *N Engl J Med*, 2012, 367(5):423-34. [PubMed [22784038](#)]
10. www.uptodate.com: Tenofovir and emtricitabine: Drug Information
11. www.epocrates.com: Truvada Drug Information

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1/24/17	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
1/23/18	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
1/22/19	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
1/26/19	Yes	Catherine Sanders, MD; Robert Sterling, MD	Update: Removed the requirement that Truvada be prescribed by an Immunology Clinic physician with current American academy of HIV Medicine (AAHIVM) certification or a physician boarded in Infectious Disease for PrEP. Added additional criteria requirements for PrEP.
6/19/19	Yes	Howard Taekman, MD	Updated to add that PCPs can prescribe Truvada for PEP and Note: Recommended as first-line therapy for PEP in combination with raltegravir (Isentress) in antiretroviral naive patients.

2/18/20	No	Howard Taekman, MD; Robert Sterling, MD	Annual review

Agreement Form

**for Initiating Emtricitabine/Tenofovir
Disoproxil Fumarate 200 mg/300 mg for HIV-1
Pre-exposure Prophylaxis (PrEP)**

Individual Label

Instructions: Review form with an HIV-negative person who is about to start or is taking emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP at each visit. File form in the person's medical record.

Emtricitabine/tenofovir disoproxil fumarate is indicated in combination with safer sex practices for HIV-1 pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in at-risk adults and adolescents weighing at least 35 kg. Individuals must have a negative HIV-1 test immediately prior to initiating emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP.

- 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 cleared by the FDA as an aid in the diagnosis of HIV-1 infection, including acute or primary HIV-1 infection

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

- Has partner(s) known to be HIV-1 infected, or
- Engages in sexual activity within a high prevalence area or social network and has additional risk factors for HIV-1 acquisition, such as:
 - Inconsistent or no condom use
 - Diagnosis of sexually transmitted infections
 - Exchange of sex for commodities (such as money, shelter, food, or drugs)
 - Use of illicit drugs, alcohol dependence
 - Incarceration
 - Partner(s) of unknown HIV-1 status with any of the factors listed above

Healthcare Provider Agreement

By signing below, I signify my understanding of the risks and benefits of emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP and my obligation as a prescriber to educate the HIV-negative person about these risks, counsel the person on risk reduction, monitor the person appropriately, and report adverse events. Specifically, I attest to having done the following:

- Confirmed the negative HIV-1 status of this person prior to starting emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP
- Read the Prescribing Information, including the BOXED WARNING
- Discussed with the HIV-negative person the known safety risks with use of emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP
- Reviewed the importance of adherence with a comprehensive prevention strategy, including practicing safer sex
- Discussed the importance of virologic suppression in their partner(s) with HIV
- Discussed the importance of regular HIV-1 testing (at least every 3 months) while taking emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP, noting that some individuals, such as adolescents, may benefit from more frequent visits and counseling
- Reviewed the emtricitabine/tenofovir disoproxil fumarate Medication Guide with the HIV-negative person at risk prior to prescribing emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP
- Completed the items on the Checklist for Prescribers: Initiation of Emtricitabine/Tenofovir Disoproxil Fumarate for HIV-1 Pre-exposure Prophylaxis (PrEP)

Healthcare Provider's Signature

Date

HIV-Negative Person Agreement

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

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

HIV-Negative Person's Signature

Date

Checklist for Prescribers: Initiation of Emtricitabine/ Tenofovir Disoproxil Fumarate 200 mg/300 mg for HIV-1 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 emtricitabine/tenofovir disoproxil fumarate for HIV-1 pre-exposure prophylaxis (PrEP) for the adult or adolescent weighing at least 35 kg who is about to start or is taking emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP:

Lab Tests/Evaluation

- ☐ Completed risk evaluation of uninfected individual
- ☐ Confirmed a negative HIV-1 test immediately prior to initiating emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP
 - If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposure is suspected, delay starting HIV-1 PrEP for at least 1 month and reconfirm HIV-1 status or use a test approved or cleared by the FDA as an aid in the diagnosis of HIV-1 infection, including acute or primary HIV-1 infection. (Note: emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP is contraindicated in individuals with unknown HIV-1 status or who are HIV-1 positive)
- ☐ Performed HBV screening test
- ☐ Confirmed estimated creatinine clearance (CrCl) ≥ 60 mL/min prior to initiation and periodically during treatment
- ☐ On a clinically appropriate schedule, assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein in all patients before initiation of emtricitabine/tenofovir disoproxil fumarate and periodically while emtricitabine/tenofovir disoproxil fumarate is being used. In patients with chronic kidney disease, also assess serum phosphorus. If a decrease in estimated CrCl is observed in uninfected individuals while using emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP, evaluate potential causes and re-assess potential risks and benefits of continued use
- ☐ Confirmed that the uninfected at-risk individual is not taking other HIV-1 medications or HBV medications
- ☐ Evaluated risk/benefit for women who may be pregnant or may want to become pregnant

Counseling/Follow-up

- ☐ Discussed known safety risks with use of emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP
- ☐ Counselor 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 emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP to reconfirm HIV-1-negative status
 - Some individuals, such as adolescents, may benefit from more frequent visits and counseling
- ☐ Discussed the importance of discontinuing emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP if seroconversion has occurred, to reduce the development of resistant HIV-1 variants
- ☐ Counselor on the importance of adherence to daily dosing schedule
- ☐ Counselor that emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP 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 virologic suppression in partner(s) with HIV
- ☐ Discussed the importance of and performed screening for sexually transmitted infections (STIs), such as syphilis, chlamydia, and gonorrhea, that can facilitate HIV-1 transmission
- ☐ Offered HBV vaccination as appropriate
- ☐ Provided education on where information about emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP can be accessed
- ☐ Discussed potential adverse reactions
- ☐ Reviewed the Emtricitabine/Tenofovir Disoproxil Fumarate Medication Guide with the uninfected at-risk individual

**Emtricitabine/Tenofovir Disoproxil
Fumarate 200 mg/300 mg for HIV-1
Pre-exposure Prophylaxis (PrEP)**

Training Guide for Healthcare Providers

About emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP to reduce the risk of sexually acquired HIV-1 infection in at-risk adults and adolescents weighing at least 35 kg

INDICATION

Emtricitabine/tenofovir disoproxil fumarate is indicated in combination with safer sex practices for HIV-1 pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in at-risk adults and adolescents weighing at least 35 kg.* Individuals must have a negative HIV-1 test immediately prior to initiating emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP.

- If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposures are suspected, delay starting HIV-1 PrEP for at least 1 month and reconfirm HIV-1 status or use a test cleared by the FDA as an aid in the diagnosis of HIV-1 infection, including acute or primary HIV-1 infection

PRESCRIBING CONSIDERATIONS: When prescribing emtricitabine/tenofovir disoproxil fumarate for pre-exposure prophylaxis:

- Only prescribe emtricitabine/tenofovir disoproxil fumarate as part of a comprehensive prevention strategy because emtricitabine/tenofovir disoproxil fumarate is not always effective in preventing the acquisition of HIV-1
- Counsel all uninfected individuals to strictly adhere to their emtricitabine/tenofovir disoproxil fumarate daily dosing schedule because the effectiveness of emtricitabine/tenofovir disoproxil fumarate in reducing the risk of acquiring HIV-1 is strongly correlated with adherence and measurable drug levels

*Factors that may help to identify individuals at 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.

- Confirm a negative HIV-1 test immediately prior to initiating emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP. If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposures are suspected, delay starting HIV-1 PrEP for at least 1 month and reconfirm HIV-1 status or use a test cleared by the FDA as an aid in the diagnosis of HIV-1 infection, including acute or primary HIV-1 infection
- Screen uninfected individuals for HIV-1 infection at least once every 3 months while taking emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP. Some individuals, such as adolescents, may benefit from more frequent visits and counseling
- Do not prescribe emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP if signs or symptoms of acute HIV-1 infection are present unless negative infection status is confirmed

The following points should also be considered when prescribing emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP in adolescents:

- Use of emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP as part of a comprehensive HIV prevention strategy for adolescents should include consideration of the ability of the individual to understand the importance of adherence to daily dosing, the need for frequent HIV testing, the need for frequent sexually transmitted infection testing, and the continued risk of pregnancy
- In a clinical study in adolescents, the percentage of subjects with protective levels of drug declined markedly after subjects switched from monthly to quarterly visits, suggesting that adolescents may benefit from more frequent visits and counseling

BOXED WARNING:

- Emtricitabine/tenofovir disoproxil fumarate used for HIV-1 PrEP 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 emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP following undetected acute HIV-1 infection. Do not initiate emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP if signs or symptoms of acute HIV-1 infection are present unless negative infection status is confirmed
- Severe acute exacerbations of hepatitis B virus (HBV) have been reported in HBV-infected patients who have discontinued emtricitabine/tenofovir disoproxil fumarate. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in HBV-infected patients who discontinue emtricitabine/tenofovir disoproxil fumarate. If appropriate, initiation of anti-hepatitis B therapy may be warranted

Why Use Emtricitabine/Tenofovir Disoproxil Fumarate for HIV-1 PrEP?

By inhibiting HIV-1 from replicating as it enters the body, emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP works to prevent the virus from establishing permanent infection. However, emtricitabine/tenofovir disoproxil fumarate should not be seen as the first line of defense against HIV-1 infection. Because emtricitabine/tenofovir disoproxil fumarate is not always effective in preventing the acquisition of HIV-1 infection, emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP 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 partner[s]), and other proven HIV-1 prevention methods to safely and effectively reduce the risk of acquiring HIV-1 infection.

- Emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP must only be prescribed to uninfected individuals at risk who are confirmed to be HIV-1 negative
- Uninfected individuals who are prescribed emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP should not miss any doses. Missing doses raises the risk of acquiring HIV-1 infection

Emtricitabine/tenofovir disoproxil fumarate is also indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection. Emtricitabine/tenofovir disoproxil fumarate should never be used alone in an individual infected with HIV-1 because of the increased risk of resistance. Therefore, it is critical to confirm negative HIV-1 status immediately prior to initiating emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP. If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposures are suspected, delay starting HIV-1 PrEP for at least 1 month and reconfirm HIV-1 status or use a test approved or cleared 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 emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP. Some individuals, such as adolescents, may benefit from more frequent visits and counseling.

Key Findings of the Emtricitabine/Tenofovir Disoproxil Fumarate for HIV-1 PrEP Trials

The iPrEx Trial

- In one clinical trial of emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP, emtricitabine/tenofovir disoproxil fumarate was shown to reduce the risk of HIV-1 infection acquisition by 42% for high-risk adult men who have sex with men who also received comprehensive prevention services, including monthly HIV-1 testing, condom provision, risk-reduction 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
- Intensive risk reduction counseling was provided as part of the trial, and 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 emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP in adult serodiscordant couples, emtricitabine/tenofovir disoproxil fumarate was shown to reduce HIV-1 infection acquisition by 75% for the uninfected individuals exposed to the virus through heterosexual sex
- In a post hoc case control study of plasma drug levels in about 10% of clinical trial subjects, risk reduction appeared to be the greatest in subjects with detectable plasma tenofovir. Efficacy was therefore strongly correlated with adherence

The ATN 113 Trial

- Safety, adherence, and resistance were evaluated in a single-arm, open-label clinical trial (ATN 113) in which 67 HIV-1 uninfected adolescent men who have sex with men received emtricitabine/tenofovir disoproxil fumarate once daily for HIV-1 PrEP
- In the ATN 113 trial, HIV-1 seroconversion occurred in three subjects. Tenofovir diphosphate (DP) levels in dried blood spot assays indicate that these subjects had poor adherence
- Adherence to study drug, as measured by tenofovir DP levels in dried blood spot assays, declined markedly after Week 12 once subjects switched from monthly to quarterly visits, suggesting that adolescents may benefit from more frequent visits and counseling

Emtricitabine/Tenofovir Disoproxil Fumarate Safety Profile

IMPORTANT SAFETY INFORMATION

Contraindications

- Emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP is contraindicated in individuals with positive or unknown HIV-1 status

Warnings and Precautions

Comprehensive Management to Reduce the Risk of Acquiring HIV-1 and Development of HIV-1 Resistance

Use emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP only as part of a comprehensive prevention strategy that includes other prevention measures, such as safer sex practices, because emtricitabine/tenofovir disoproxil fumarate is not always effective in preventing the acquisition of HIV-1.

- Counsel uninfected individuals about safer sex practices, including:
 - Using condoms consistently and correctly
 - Knowing their HIV-1 status and that of their partner(s)
 - The importance of virologic suppression in their partner(s) with HIV-1
 - Being regularly tested for other sexually transmitted infections that can facilitate HIV-1 transmission (e.g., syphilis, chlamydia, and gonorrhea)
- Informing individuals about the importance of reducing sexually risky behaviors and supporting their efforts to do so
- **Use emtricitabine/tenofovir disoproxil fumarate 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 emtricitabine/tenofovir disoproxil fumarate because emtricitabine/tenofovir disoproxil fumarate alone does not constitute a complete treatment regimen for HIV-1 infection. Therefore, care should be taken to minimize drug exposure in HIV-1 infected individuals:
 - Confirm a negative HIV-1 test immediately prior to initiating emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP
 - 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 emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP, evaluate seronegative individuals for current or recent signs or symptoms consistent with acute viral infections (e.g., fever, fatigue, myalgia, skin rash) 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
 - If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposures are suspected, delay starting HIV-1 PrEP for at least 1 month and reconfirm HIV-1 status or use a test approved or cleared by the FDA as an aid in the diagnosis of HIV-1 infection, including acute or primary HIV-1 infection
- While using emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP, HIV-1 screening tests should be repeated at least every 3 months, and upon diagnosis of any sexually transmitted infections. Some individuals, such as adolescents, may benefit from more frequent visits and counseling
- If a screening test indicates possible HIV-1 infection, or if symptoms consistent with acute HIV-1 infection develop following a potential exposure event, convert the HIV-1 PrEP regimen to an HIV treatment regimen until negative infection status is confirmed using a test approved or cleared 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 emtricitabine/tenofovir disoproxil fumarate daily dosing schedule. The effectiveness of emtricitabine/tenofovir disoproxil fumarate in reducing the risk of acquiring HIV-1 is strongly correlated with adherence, as demonstrated by measurable drug levels in clinical trials
- **New onset or worsening renal impairment:**
 - Can include acute renal failure and Fanconi syndrome (renal tubular injury with severe hypophosphatemia)
 - Prior to initiating and during use of emtricitabine/tenofovir disoproxil fumarate, on a clinically appropriate schedule, assess serum creatinine, estimated creatinine clearance (CrCl), urine glucose, and urine protein in all patients. In patients with chronic kidney disease, also assess serum phosphorus
 - Emtricitabine/tenofovir disoproxil fumarate should be avoided with concurrent or recent use of a nephrotoxic agent (e.g., high-dose or multiple non-steroidal anti-inflammatory drugs [NSAIDs]). Cases of acute renal failure after initiation of high-doses or multiple NSAIDs have been reported. Some patients required hospitalization and renal replacement therapy. Alternatives to NSAIDs should be considered, if needed, in patients at risk for renal dysfunction

- Emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP is not recommended in uninfected individuals with an estimated CrCl below 60 mL/min

- If a decrease in estimated CrCl is observed while using emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP, evaluate potential causes and reassess potential risks and benefits of continued use

- **HBV infection:**

- All patients should be tested for chronic hepatitis B virus (HBV)
 - HBV-uninfected individuals should be offered vaccination
 - HBV-infected individuals should be monitored closely for exacerbations of hepatitis B for at least several months after discontinuing emtricitabine/tenofovir disoproxil fumarate (see **BOXED WARNING** above)

- **Lactic acidosis/severe hepatomegaly with steatosis:** Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported. Discontinue treatment in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity

- **Bone effects:**

- Decreases in bone mineral density (BMD) and mineralization defects, including osteomalacia, have been seen in patients treated with tenofovir disoproxil fumarate. Consider assessment of BMD in individuals with a history of pathologic fracture or other risk factors for osteoporosis or bone loss
 - Persistent or worsening bone pain, pain in extremities, fractures, and/or muscular pain or weakness may be manifestations of proximal renal tubulopathy and should prompt an evaluation of renal function in at-risk patients

- **Coadministration with other products:** Do not use emtricitabine/tenofovir disoproxil fumarate with drugs containing emtricitabine, tenofovir disoproxil fumarate, or tenofovir alafenamide, with drugs containing lamivudine, or with adefovir dipivoxil

Important Safety Information

Common Adverse Events

- In HIV-1 uninfected adults in PrEP trials, adverse reactions that were reported by more than 2% of emtricitabine/tenofovir disoproxil fumarate subjects and more frequently than by placebo subjects were headache, abdominal pain, and decreased weight

Important Safety Information About the Use of Emtricitabine/Tenofovir Disoproxil Fumarate for HIV-1 PrEP in Specific Populations

- **Pregnancy:**

- Data on the use of emtricitabine/tenofovir disoproxil fumarate during pregnancy from observational studies have shown no increased risk of major birth defects
 - Published studies indicate an increased risk of HIV-1 infection during pregnancy and an increased risk of mother-to-child transmission during acute HIV-1 infection. In women at risk of acquiring HIV-1, consideration should be given to methods to prevent acquisition of HIV, including continuing or initiating emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP, during pregnancy
 - A pregnancy registry is available. Enroll pregnant women exposed to emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP by calling the Antiretroviral Pregnancy Registry (APR) at 1-800-258-4263

• **Lactation:**

- It is not known if the components of emtricitabine/tenofovir disoproxil fumarate (emtricitabine and tenofovir disoproxil fumarate) affect milk production or have effects on the breastfed child
- In HIV-1–uninfected women, the developmental and health benefits of breastfeeding and the mother’s clinical need for emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP should be considered along with any potential adverse effects on the breastfed child from emtricitabine/tenofovir disoproxil fumarate and the risk of HIV-1 acquisition due to nonadherence and subsequent mother-to-child transmission
- Women should not breastfeed if acute HIV-1 infection is suspected because of the risk of HIV-1 transmission to the infant

• **Pediatrics:**

- Safety, adherence, and resistance were evaluated in a single-arm, open-label clinical trial (ATN 113) of 67 HIV-1 uninfected at-risk adolescent men who have sex with men received emtricitabine/tenofovir disoproxil fumarate once daily for HIV-1 PrEP
- In the ATN 113 trial, HIV-1 seroconversion occurred in 3 subjects. Tenofovir diphosphate (DP) levels in dried blood spot assays indicate that these subjects had poor adherence
- Adherence to study drug, as demonstrated by tenofovir DP levels in dried blood spot assays, declined markedly after Week 12 once subjects switched from monthly to quarterly visits, suggesting that adolescents may benefit from more frequent visits and counseling

Reminder About the Use of Emtricitabine/Tenofovir Disoproxil Fumarate for HIV-1 PrEP: Confirming and Regularly Reconfirming Negative HIV-1 Status

- Emtricitabine/tenofovir disoproxil fumarate should be used to reduce the risk of acquiring HIV-1 infection only in individuals confirmed to be HIV-1 negative
- A negative HIV-1 status should be confirmed before prescribing emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP
- Individuals should be regularly tested (at least every 3 months) while taking emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP. Some individuals, such as adolescents, may benefit from more frequent visits and counseling
- If a screening test indicates possible infection, or symptoms consistent with acute HIV-1 infection develop following a potential exposure event, convert the HIV-1 PrEP regimen to an HIV treatment regimen until negative infection status is confirmed using a test approved or cleared 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 emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP

Drug Interactions

- Coadministration of emtricitabine/tenofovir disoproxil fumarate with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of tenofovir

For further details about emtricitabine/tenofovir disoproxil fumarate drug interactions, please see Prescribing Information for emtricitabine/tenofovir disoproxil fumarate in back pocket.

Use the Checklist for Prescribers: Initiation of Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg for HIV-1 Pre-exposure Prophylaxis (PrEP) and the Agreement Form for Initiating Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg for HIV-1 Pre-exposure Prophylaxis (PrEP) to help manage and counsel individuals about the correct and safe use of emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP.

For more information about emtricitabine/tenofovir disoproxil fumarate and its indication for HIV-1 PrEP, please see the Prescribing Information, including the BOXED WARNING, and the Medication Guide. For more information about the REMS program for emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP, please log on to www.ftc-tdf-preprems.com. You may also obtain additional information and educational materials about the use of emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP at 1-800-625-7471.

Post-Training Review Questions

1. Emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP should be used only:

- a. As part of a comprehensive HIV-1 prevention strategy that includes other preventive measures since emtricitabine/tenofovir disoproxil fumarate is not always effective in preventing the acquisition of HIV-1 infection
- b. In individuals who have been counseled to strictly adhere to their emtricitabine/tenofovir disoproxil fumarate daily dosing schedule since the effectiveness of emtricitabine/tenofovir disoproxil fumarate in reducing the risk of acquiring HIV-1 infection is strongly correlated with adherence and measurable drug levels
- c. In individuals who have a confirmed negative HIV-1 test prior to initiating and routinely while taking emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP
- d. All of the above

2. Which of the following statements is false?

- a. Emtricitabine/tenofovir disoproxil fumarate should be used for HIV-1 PrEP only in individuals confirmed to be HIV-1 negative
- b. Emtricitabine/tenofovir disoproxil fumarate is indicated for HIV-1 PrEP to reduce the risk of acquiring HIV-1 infection through injection drug use
- c. Women taking emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP should not breastfeed their babies if acute HIV-1 infection is suspected
- d. Emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP is not always effective in preventing HIV-1 infection

3. Which of the following items are not included on the Checklist for Prescribers: Initiation of Emtricitabine/Tenofovir Disoproxil Fumarate for HIV-1 Pre-exposure Prophylaxis (PrEP)?

- 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

4. Hepatic function should be monitored closely in:

- a. HBV-infected individuals who discontinue emtricitabine/tenofovir disoproxil fumarate
- b. All people taking emtricitabine/tenofovir disoproxil fumarate
- c. All people who discontinue emtricitabine/tenofovir disoproxil fumarate
- d. None of the above

5. In clinical trials evaluating emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP, which of the following adverse reactions was not common?

- a. Abdominal pain
- b. Headache
- c. Dizziness
- d. Decreased weight

6. Emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP is indicated only for:

- a. Men who are at risk for sexually acquired HIV-1 infection
- b. Adults and adolescents weighing at least 35 kg who are at risk of acquiring HIV-1 infection by any means
- c. Adults and adolescents weighing at least 35 kg who are at risk of acquiring HIV-1 infection through injection drug use
- d. Adults and adolescents weighing at least 35 kg who are at risk for sexually acquired HIV-1 infection

7. The Agreement Form for Initiating Emtricitabine/Tenofovir Disoproxil Fumarate for HIV-1 Pre-exposure Prophylaxis (PrEP) provides which of the following information:

- a. A list of activities that put individuals at risk for sexually acquired HIV-1 infection
- b. A confirmation that the prescriber has discussed the risks and benefits of using emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP with the uninfected individual
- c. A signature from the individual asserting that the prescriber has explained the risks and benefits of taking emtricitabine/tenofovir disoproxil fumarate for HIV-1 PrEP, including the need for adherence and a comprehensive prevention strategy, which includes safer sex practices
- d. All of the above

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

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Reference ID: 4262803

**Help uninfected individuals learn more
about emtricitabine/tenofovir disoproxil
fumarate for HIV-1 pre-exposure
prophylaxis (PrEP)**



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Reference: TRUVADA [package insert]. Foster City, CA:
Gilead Sciences, Inc; 2018.

RCMS-SSS-0028 05/18

Reference ID: 4262803