Important safety Information for prescribers

About Emtricitabine/Tenofovir disoproxil Teva for a Pre-Exposure Prophylaxis (PrEP) Indication

Emtricitabine/Tenofovir disoproxil Teva (emtricitabine/tenofovir disoproxil) is indicated in combination with safer sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection in adults at high risk.

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Key safety information regarding the use of Emtricitabine/Tenofovir disoproxil Teva for PrEP

- Emtricitabine/Tenofovir disoproxil Teva should only be used to reduce the risk of acquiring HIV-1 in individuals confirmed to be HIV-negative prior to initiating Emtricitabine/Tenofovir disoproxil Teva for PrEP and re-confirmed at frequent intervals (e.g. at least every 3 months) while taking Emtricitabine/Tenofovir disoproxil Teva for PrEP, using a combined antigen/antibody test.
- HIV-1 resistance mutations have emerged in individuals with undetected HIV-1 infection who were only taking Emtricitabine/Tenofovir disoproxil Teva.
- Emtricitabine/Tenofovir disoproxil Teva should only be used as part of a comprehensive prevention strategy because Emtricitabine/Tenofovir disoproxil Teva is not always effective in preventing the acquisition of HIV-1 infection.
- Do not initiate (or re-initiate) Emtricitabine/Tenofovir disoproxil Teva for PrEP if signs or symptoms of acute HIV infection are present unless negative infection status is confirmed.
- Counsel HIV-1-uninfected individuals to strictly adhere to the recommended Emtricitabine/Tenofovir disoproxil Teva dosing schedule.
- Do not prescribe Emtricitabine/Tenofovir disoproxil Teva to uninfected individuals with a creatinine clearance (CrCl) below 60 mL/min and only use Emtricitabine/Tenofovir disoproxil Teva in individuals with CrCl <80 mL/min if the potential benefits are considered to outweigh the potential risks. Renal function should be regularly monitored while taking Emtricitabine/Tenofovir disoproxil Teva for PrEP.

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Factors to help identify individuals at high risk of acquiring HIV-1

Has partner(s) known to be HIV-1 infected who is not on antiretroviral treatment, 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 or alcohol dependence
- Incarceration
- Partner(s) of unknown HIV-1 status with any of the factors listed above

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Risk of development of HIV-1 drug resistance in undiagnosed HIV-1-infected individuals

Emtricitabine/Tenofovir disoproxil Teva for a PrEP indication is contraindicated in individuals with unknown or HIV-1-positive status.

- Use Emtricitabine/Tenofovir disoproxil Teva to reduce the risk of acquiring HIV-1 infection only in individuals confirmed to be HIV-1 negative. Emtricitabine/Tenofovir disoproxil Teva alone does not constitute a complete treatment regimen for HIV-1 infection and HIV-1 resistance substitutions may emerge in individuals with undetected HIV-1 infection who are taking only Emtricitabine/Tenofovir disoproxil Teva.

Before starting Emtricitabine/Tenofovir disoproxil Teva for PrEP:

- Confirm a negative HIV-1 test, using a combined antigen/antibody test.
- If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposures are suspected, delay starting Emtricitabine/Tenofovir disoproxil Teva for a PrEP indication for at least 1 month and reconfirm HIV-1 status.

During use of Emtricitabine/Tenofovir disoproxil Teva for PrEP:

- Screen for HIV-1 infection at frequent intervals (e.g. at least every 3 months) using a combined antigen/antibody test.
- If symptoms consistent with acute HIV-1 infection develop following a potential exposure event, Emtricitabine/Tenofovir disoproxil Teva should be discontinued until negative infection status is confirmed.

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Only use Emtricitabine/Tenofovir disoproxil Teva for PrEP as part of a comprehensive prevention strategy

Emtricitabine/Tenofovir disoproxil Teva for a PrEP indication should be used only as part of an overall HIV-1 infection prevention strategy including the use of other HIV-1 infection prevention measures, such as safer sex practices, because Emtricitabine/Tenofovir disoproxil Teva is not always effective in preventing the acquisition of HIV-1 infection. The time to onset of protection after commencing Emtricitabine/Tenofovir disoproxil Teva is unknown.

Counsel uninfected individuals at high risk about safer sex practices, including:

- Using condoms consistently and correctly.
- Knowing their HIV-1 status and that of their partner(s).
- Being regularly tested for other sexually transmitted infections that can facilitate HIV-1 transmission (e.g. syphilis and gonorrhoea).

The importance of strict adherence to the recommended dosing regimen

The effectiveness of Emtricitabine/Tenofovir disoproxil Teva for a PrEP indication in reducing the risk of acquiring HIV-1 infection is strongly correlated with adherence as demonstrated by measurable drug levels in blood.

- The recommended dose of Emtricitabine/Tenofovir disoproxil Teva is one tablet, once daily.
- All uninfected individuals at high risk taking Emtricitabine/Tenofovir disoproxil for a PrEP indication should be counselled to strictly adhere to the recommended Emtricitabine/Tenofovir disoproxil Teva dosing schedule to reduce the risk of acquiring HIV-1 infection.
- All uninfected individuals at high risk taking Emtricitabine/Tenofovir disoproxil Teva for a PrEP indication should be supplied with a PrEP educational brochure prior to initiation of treatment and a PrEP reminder card when each new bottle of Emtricitabine/Tenofovir disoproxil Teva is supplied to the individual.

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Emtricitabine/Tenofovir disoproxil Teva related renal toxicity

Renal failure, renal impairment, elevated creatinine, hypophosphatemia and proximal tubulopathy (including Fanconi syndrome) have been reported with the use of tenofovir disoproxil, a component of Emtricitabine/Tenofovir disoproxil Teva.

- Assess estimated creatinine clearance (CrCl) in all individuals before prescribing Emtricitabine/Tenofovir disoproxil Teva.
- In individuals without renal risk factors, renal function (CrCl and serum phosphate) should also be monitored after 2 to 4 weeks of use, after 3 months of use and every 3 to 6 months thereafter. In individuals at risk for renal impairment, a more frequent monitoring of renal function is required.
- Avoid administering Emtricitabine/Tenofovir disoproxil Teva with concurrent or recent use of nephrotoxic drugs. If concomitant use of Emtricitabine/Tenofovir disoproxil Teva and nephrotoxic agents is unavoidable, renal function should be monitored weekly.
- Cases of acute renal failure have been reported after initiation of high-dose or multiple non-steroidal anti-inflammatory drugs (NSAIDs) in HIV-1-infected patients treated with tenofovir disoproxil and with risk factors for renal dysfunction.
  If Emtricitabine/Tenofovir disoproxil Teva is co-administered with an NSAID, renal function should be monitored adequately.
- Emtricitabine/Tenofovir disoproxil Teva should only be used in individuals with CrCl <80mL/min if the potential benefits are considered to outweigh the potential risks.

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- If serum phosphate is <1.5 mg/dL (0.48 mmol/L) or CrCl is decreased to <60 mL/min in any individual receiving Emtricitabine/Tenofovir disoproxil Teva for PrEP, renal function should be re-evaluated within 1 week, including measurements of blood glucose, blood potassium and urine glucose concentrations

- Consideration should be given to interrupting use of Emtricitabine/Tenofovir disoproxil Teva in individuals with CrCl decreased to <60 mL/min or decreases in serum phosphate to <1.0 mg/dL (0.32 mmol/L)

- Interrupting use of Emtricitabine/Tenofovir disoproxil Teva should also be considered in case of progressive decline of renal function when no other cause has been identified

- **Do not prescribe Emtricitabine/Tenofovir disoproxil Teva for PrEP to individuals with an estimated CrCl below 60 mL/min**

Bone effects

- Small decreases in bone mineral density (BMD) have been seen in uninfected individuals receiving Emtricitabine/Tenofovir disoproxil Teva.
  - If bone abnormalities are suspected then appropriate consultation should be obtained.

HBV infection

There is a risk of severe acute exacerbation of hepatitis when individuals with hepatitis B infection stop taking Emtricitabine/Tenofovir disoproxil Teva.
As a result, it is recommended that:

- Individuals infected with HBV who discontinue Emtricitabine/Tenofovir disoproxil Teva should be closely monitored with both clinical and laboratory follow-up for at least several months after stopping treatment.
- All individuals be tested for the presence of current HBV before initiating Emtricitabine/Tenofovir disoproxil Teva.
- HBV-uninfected individuals should be offered vaccination.

Use of Emtricitabine/Tenofovir disoproxil Teva for a PrEP indication in pregnancy

The balance of risks and benefits for women who may be pregnant or may want to become pregnant should be evaluated, if applicable. Prescribers are encouraged to enroll women exposed to Emtricitabine/Tenofovir disoproxil Teva for PrEP during pregnancy to the Antiretroviral Pregnancy Registry at www.apregistry.com. The Registry aims to detect any major teratogenic effects involving antiretroviral agents to which pregnant women are exposed.

Any suspected adverse reactions to Emtricitabine/Tenofovir disoproxil Teva should be reported to Teva via email to safety.ireland@teva.ie or by telephone to +44 (1) 207 540 7117.
You can also report side effects directly via the national reporting system:
HPRA Pharmacovigilance, Earlsfort Terrace, Dublin, Ireland. Tel +353 1 6764971;
Fax +353 1 6762517; Email: medsafety@hpra.ie; Website: www.hpra.ie.

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