



## IMPORTANT SAFETY INFORMATION

### **For Prescribers About Emtricitabine/tenofovir disoproxil Rowex for a Pre-Exposure Prophylaxis (PrEP) Indication**

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

### Key safety information regarding the use of Emtricitabine/tenofovir disoproxil Rowex for PrEP

- Emtricitabine/tenofovir disoproxil Rowex 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 Rowex for PrEP and re-confirmed at frequent intervals (e.g. at least every 3 months) while taking Emtricitabine/tenofovir disoproxil Rowex 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
- Emtricitabine/tenofovir disoproxil Rowex should only be used as part of a comprehensive prevention strategy because Emtricitabine/tenofovir disoproxil Rowex is not always effective in preventing the acquisition of HIV-1 infection
- Do not initiate (or re-initiate) Emtricitabine/tenofovir disoproxil Rowex 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 Rowex dosing schedule
- Do not prescribe Emtricitabine/tenofovir disoproxil Rowex to uninfected individuals with an estimated creatinine clearance (CrCl) below 60 mL/min and only use Emtricitabine/tenofovir disoproxil Rowex 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 Rowex for PrEP

### 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

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

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

- Use Emtricitabine/tenofovir disoproxil Rowex to reduce the risk of acquiring HIV-1 infection only in individuals confirmed to be HIV-1 negative. Emtricitabine/tenofovir disoproxil Rowex 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 Rowex
- **Before starting Emtricitabine/tenofovir disoproxil Rowex 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 Rowex for a PrEP indication for at least 1 month and reconfirm HIV-1 status
- **During use of Emtricitabine/tenofovir disoproxil Rowex 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 Rowex should be discontinued until negative infection status is confirmed

## Only use Emtricitabine/tenofovir disoproxil Rowex for PrEP as part of a comprehensive prevention strategy

Emtricitabine/tenofovir disoproxil Rowex 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 Rowex is not always effective in preventing the acquisition of HIV-1 infection. The time to onset of protection after commencing Emtricitabine/tenofovir disoproxil Rowex 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 Rowex 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 Rowex is one tablet, once daily.
- All uninfected individuals at high risk taking Emtricitabine/tenofovir disoproxil Rowex for a PrEP indication should be counselled to strictly adhere to the recommended Emtricitabine/tenofovir disoproxil Rowex dosing schedule to reduce the risk of acquiring HIV-1 infection
- All uninfected individuals at high risk taking Emtricitabine/tenofovir disoproxil Rowex 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 Rowex is supplied to the individual

## Emtricitabine/tenofovir disoproxil Rowex 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 fumarate, a component of Emtricitabine/tenofovir disoproxil Rowex.**

- Assess estimated creatinine clearance (CrCl) in all individuals before prescribing Emtricitabine/tenofovir disoproxil Rowex
- 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 Rowex with concurrent or recent use of nephrotoxic drugs. If concomitant use of Emtricitabine/tenofovir disoproxil Rowex 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 fumarate and with risk factors for renal dysfunction. If Emtricitabine/tenofovir disoproxil Rowex is co-administered with an NSAID, renal function should be monitored adequately
- **Do not prescribe Emtricitabine/tenofovir disoproxil Rowex for PrEP to individuals with an estimated CrCl below 60 mL/min**

- Emtricitabine/tenofovir disoproxil Rowex should only be used in individuals with CrCl  $<80$  mL/min if the potential benefits are considered to outweigh the potential risks
- 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 Rowex 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 Rowex 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 Rowex should also be considered in case of progressive decline of renal function when no other cause has been identified

## Bone effects

- Small decreases in bone mineral density (BMD) have been seen in uninfected individuals receiving Emtricitabine/tenofovir disoproxil
  - 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. As a result, it is recommended that:

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

## Use of Emtricitabine/tenofovir disoproxil Rowex 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 Rowex for PrEP during pregnancy to the Antiretroviral Pregnancy Registry at [www.apregistry.com](http://www.apregistry.com). The Registry aims to detect any major teratogenic effects involving antiretroviral agents to which pregnant women are exposed.

**For more information about Emtricitabine/tenofovir disoproxil Rowex and its indication for PrEP, please refer to the Summary of Product Characteristics**

Please report any adverse events suspected to be caused by the use of Emtricitabine/tenofovir disoproxil Rowex to Rowex Ltd, Bantry, Co.Cork. Tel 027 50077; fax 027 50417 or the HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: [www.hpra.ie](http://www.hpra.ie); E-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie)