Important Safety Information About PrMINT-EMTRICITABINE/TENOFOVIR for a Pre-exposure Prophylaxis (PrEP) Indication

For Healthcare Providers

About MINT-EMTRICITABINE/TENOFOVIR for a PrEP Indication in adults at high risk

Indication and Prescribing Considerations

MINT-EMTRICITABINE/TENOFOVIR (emtricitabine/tenofovir disoproxil fumarate), 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

The following points must be considered when prescribing MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication:

- Only prescribe MINT-EMTRICITABINE/TENOFOVIR as part of a comprehensive prevention strategy because MINT-EMTRICITABINE/TENOFOVIR is not always effective in preventing the acquisition of HIV-1 infection
- Counsel all uninfected individuals to strictly adhere to their MINT-EMTRICITABINE/TENOFOVIR daily dosing schedule because the effectiveness of MINT-EMTRICITABINE/TENOFOVIR in reducing the risk of acquiring HIV-1 infection was strongly correlated with adherence as demonstrated by measurable drug levels in clinical trials
- Confirm a negative HIV-1 test immediately prior to initiating MINT-EMTRICITABINE/TENOFOVIR 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 Health Canada 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 MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication
- Do not prescribe MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication if signs or symptoms of acute HIV-1 infection are present unless negative infection status is confirmed

Potential for Resistance in Undetected Acute HIV-1 Infection

It is important to be alert to the signs or symptoms of potential acute HIV-1 infection when prescribing MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication, including:

- Fever, headache, fatigue, arthralgia, vomiting, myalgia, diarrhea, pharyngitis, rash, night sweats, and adenopathy (cervical and inguinal)

It is recommended that negative HIV-1 status be reconfirmed on a regular basis (at least every 3 months) using HIV-1 screening tests while uninfected individuals are taking MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication.

MINT-EMTRICITABINE/TENOFOVIR Safety Profile

BOXED WARNING: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS, POST-TREATMENT ACUTE EXACERBATION OF HEPATITIS B, NEPHROTOXICITY, AND RISK OF DRUG RESISTANCE WITH USE OF MINT-EMTRICITABINE/TENOFOVIR FOR A PREP INDICATION IN UNDIAGNOSED EARLY HIV-1 INFECTION

- **MINT-EMTRICITABINE/TENOFOVIR 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 for MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication following undetected acute HIV-1 infection. Do not initiate MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication if signs or symptoms of acute HIV-1 infection are present unless negative infection status is confirmed.**
- **Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including tenofovir DF (VIREAD), a component of MINT-EMTRICITABINE/TENOFOVIR, alone or in combination with other antiretrovirals.**
- **MINT-EMTRICITABINE/TENOFOVIR is not approved for the treatment of chronic hepatitis B virus (HBV) infection and the safety and efficacy of emtricitabine and tenofovir DF have not been established in patients co-infected with HBV and HIV. Severe acute exacerbations of hepatitis B have been reported in patients co-infected with HBV and HIV who have discontinued emtricitabine and tenofovir DF. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who are co-infected with HBV and HIV and discontinue MINT-EMTRICITABINE/TENOFOVIR. If appropriate, initiation of anti-hepatitis B therapy may be warranted.**
- **Renal impairment, including cases of acute renal failure and Fanconi syndrome (renal tubular injury with severe hypophosphatemia) has been reported with the use of MINT-EMTRICITABINE/TENOFOVIR during clinical practice.**

Important Safety Information About MINT-EMTRICITABINE/TENOFOVIR for a PrEP Indication

Contraindications

- **MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication is contraindicated in individuals with positive or unknown HIV-1 status**

Warnings and Precautions

- **Comprehensive management to reduce the risk of acquiring HIV-1 infection**

  MINT-EMTRICITABINE/TENOFOVIR 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 MINT-EMTRICITABINE/TENOFOVIR is not always effective in preventing the acquisition of HIV-1.
  - Counsel uninfected individuals at high risk about safer sex practices, including:
    - Using condoms consistently and correctly
    - Knowing their HIV-1 status and that of their partner(s)
    - Being regularly tested for other sexually transmitted infections that can facilitate HIV-1 transmission (e.g., syphilis and gonorrhea)
  - Inform uninfected individuals at high risk about and support their efforts to reduce sexual risk behavior
  - Use MINT-EMTRICITABINE/TENOFOVIR 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 MINT-EMTRICITABINE/TENOFOVIR because **MINT-EMTRICITABINE/TENOFOVIR alone does not constitute a complete treatment regimen for HIV-1 infection**
  - Therefore, care should be taken to minimize drug exposure in HIV-infected individuals:
    - Confirm a negative HIV-1 test immediately prior to initiating MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication. Many HIV-1 tests, such as rapid tests, detect anti-HIV antibodies and may not identify HIV-1 during the acute stage of infection. Prior to initiating MINT-EMTRICITABINE/TENOFOVIR 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 sex, 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 MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication for at least 1 month and reconfirm HIV-1 status or use a test approved by Health Canada 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 MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication
- If symptoms consistent with acute HIV-1 infection develop following a potential exposure event, MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication should be discontinued until negative infection status is confirmed using a test approved by Health Canada as an aid in the diagnosis of HIV-1, including acute or primary HIV-1 infection
- Evaluate for signs or symptoms of acute HIV-1 infection prior to prescribing and during treatment with MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication

- Counsel all uninfected individuals to strictly adhere to a daily dosing schedule for MINT-EMTRICITABINE/TENOFOVIR. The effectiveness of MINT-EMTRICITABINE/TENOFOVIR in reducing the risk of acquiring HIV-1 was 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. Assess estimated creatinine clearance (CrCl) before prescribing and during treatment with MINT-EMTRICITABINE/TENOFOVIR. In patients at risk of renal dysfunction, monitor estimated CrCl, serum phosphorus, urine glucose and urine protein before prescribing MINT-EMTRICITABINE/TENOFOVIR and periodically while MINT-EMTRICITABINE/TENOFOVIR is being used. Avoid administering MINT-EMTRICITABINE/TENOFOVIR with concurrent or recent use of nephrotoxic drugs. There have been post marketing reports of acute renal failure in patients on concomitant NSAIDS therapy where a relationship to tenofovir DF could not be excluded. These events mostly occurred in medically complex patients, where underlying disease processes confound interpretation.
  - **For pre-exposure prophylaxis: Emtricitabine and tenofovir DF for PrEP has not been studied in HIV-1 uninfected individuals with estimated creatinine clearance below 60 mL/min. If a decrease in estimated CrCl is observed in uninfected individuals while using MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication, evaluate potential causes and reassess potential risks and benefits of continued use**
- **HBV infection:** It is recommended that all individuals be tested for the presence of chronic HBV before initiating MINT-EMTRICITABINE/TENOFOVIR
- **Redistribution/accumulation of body fat:** Observed in patients receiving antiretroviral therapy
- **Coadministration with other products:** Do not use MINT-EMTRICITABINE/TENOFOVIR with drugs containing emtricitabine or tenofovir disoproxil fumarate, with drugs containing lamivudine, or with adefovir dipivoxil

Important Safety Information

Common Adverse Reactions With MINT-EMTRICITABINE/TENOFOVIR

Selected adverse events (all grades) reported in ≥ 2% of uninfected individuals in any treatment group in the iPrEx and Partners PrEP studies:

	iPrEx Trial		Partners PrEP Trial	
	FTC/TDF N=1251	Placebo N=1248	FTC/TDF N=1579	Placebo N=1584
Gastrointestinal Disorder				
Diarrhea	7%	8%	2%	3%
Abdominal pain	4%	2%	-[a]	-
Infections and Infestations				
Pharyngitis	13%	16%	-	-
Urethritis	5%	7%	-	-
Urinary tract infection	2%	2%	5%	7%
Syphilis	6%	5%	-	-
Secondary syphilis	6%	4%	-	-
Anogenital warts	2%	3%	-	-
Musculoskeletal and Connective Tissue Disorders				
Back pain	5%	5%	-	-
Nervous System Disorders				
Headache	7%	6%	-	-
Psychiatric Disorders				
Depression	6%	7%	-	-
Anxiety	3%	3%	-	-
Reproductive System and Breast Disorders				
Genital ulceration	2%	2%	2%	2%
Investigations				
Weight decreased	3%	2%	-	-

a. Not reported or reported below 2%.

Use of MINT-EMTRICITABINE/TENOFOVIR for a PrEP Indication in Specific Populations

- **Pregnancy:** There are no adequate and well-controlled trials in pregnant women. MINT-EMTRICITABINE/TENOFOVIR should be used during pregnancy only if clearly needed. If an uninfected individual becomes pregnant while taking MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication, careful consideration should be given to whether use of MINT-EMTRICITABINE/TENOFOVIR should be continued, taking into account the potential increased risk of HIV-1 infection during pregnancy
  - A pregnancy registry is available. Enroll women taking MINT- EMTRICITABINE/TENOFOVIR for a PrEP indication by calling 1-800-258-4263
- **Nursing mothers:** The components of MINT-EMTRICITABINE/TENOFOVIR (emtricitabine/tenofovir disoproxil fumarate) are excreted in breast milk. Because the risks to the infant are not known, **mothers taking MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication should be instructed not to breastfeed.** If an uninfected individual acquires HIV-1 infection, it is recommended that she not breastfeed to avoid risking postnatal transmission of HIV-1 infection
- **Pediatrics:** Emtricitabine and tenofovir DF for a PrEP indication is based on trials in adults. Safety and effectiveness in pediatric patients have not been established.
- See Product Monograph for complete safety information

MINT-EMTRICITABINE/TENOFOVIR Drug Interactions

- Coadministration of MINT-EMTRICITABINE/TENOFOVIR with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of emtricitabine, tenofovir, and/or other renally eliminated drugs

For further details about MINT-EMTRICITABINE/TENOFOVIR drug interactions, please see the Product Monograph for MINT-EMTRICITABINE/TENOFOVIR.

Use the Checklist for Prescribers: Initiation of MINT-EMTRICITABINE/TENOFOVIR for Pre-exposure Prophylaxis (PrEP) and the Agreement Form for Initiating MINT-EMTRICITABINE/TENOFOVIR for Pre-exposure Prophylaxis (PrEP) to help manage and counsel individuals about the safe use of MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication.

MINT-EMTRICITABINE/TENOFOVIR is indicated in combination with safer sex practices for PrEP to reduce the risk of sexually acquired HIV-1 infection in adults at high risk.
Consult the product monograph at www.mintpharmaceuticals.com for contraindication, warnings, precautions, adverse reactions, interactions, dosing and conditions of clinical use. The product monograph is also available through our medical department. Call us at 1-877-398-9696