PrMINT-EMTRICITABINE/TENOFOVIR for a Pre-exposure Prophylaxis (PrEP) Indication

Training Guide for Healthcare Providers

About MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication to reduce the risk of sexually acquired HIV-1 infection in high risk adults

Indication

PrMINT-EMTRICITABINE/TENOFOVIR (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 MINT-EMTRICITABINE/TENOFOVIR for pre-exposure prophylaxis:

- 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 is strongly correlated with adherence and 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 the 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 PrEP
- Do not prescribe MINT-EMTRICITABINE/TENOFOVIR 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:

- **Lactic Acidosis and Severe Hepatomegaly with Steatosis**

  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.

- **Post-Treatment Exacerbation of Hepatitis**

  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.

- **Nephrotoxicity**

  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.

- **Risk of Drug Resistance with Use of MINT-EMTRICITABINE/TENOFOVIR for Pre-Exposure Prophylaxis (PrEP) 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 emtricitabine and tenofovir DF 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.

How does MINT-EMTRICITABINE/TENOFOVIR for PrEP work?

- Emtricitabine, a synthetic nucleoside analog of cytidine, is phosphorylated by cellular enzymes to form emtricitabine 5'-triphosphate. Emtricitabine 5'-triphosphate inhibits the activity of the HIV-1 reverse transcriptase (RT) by competing with the natural substrate deoxycytidine 5'-triphosphate and by being incorporated into nascent viral DNA which results in chain termination.
- Tenofovir disoproxil fumarate is an acyclic nucleoside phosphonate diester analog of adenosine monophosphate. Tenofovir disoproxil fumarate requires initial diester hydrolysis for conversion to tenofovir and subsequent phosphorylations by cellular enzymes to form tenofovir diphosphate. Tenofovir diphosphate inhibits the activity of HIV-1 RT by competing with the natural substrate deoxyadenosine 5'-triphosphate and, after incorporation into DNA, by DNA chain termination.

Because MINT-EMTRICITABINE/TENOFOVIR is not always effective in preventing the acquisition of HIV-1 infection, MINT-EMTRICITABINE/TENOFOVIR 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 infection.

- MINT-EMTRICITABINE/TENOFOVIR 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 MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication should not miss any doses. Missing doses raises the risk of acquiring HIV-1 infection

MINT-EMTRICITABINE/TENOFOVIR is also indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection. MINT-EMTRICITABINE/TENOFOVIR 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 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 for HIV-1 infection at least once every 3 months while taking MINT-EMTRICITABINE/TENOFOVIR for PrEP.

Key Findings of the Emtricitabine and Tenofovir DF for a PrEP Indication Trials

The iPrEx Trial

- In one clinical trial of emtricitabine and tenofovir DF for a PrEP indication, emtricitabine and tenofovir DF was shown to reduce the risk of HIV-1 infection 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 vs. placebo ((p=0.002)[†]
  - 95% Confidence Interval (18% to 60%)
  - 4237 person-years of follow up (2124 emtricitabine and tenofovir DF; 2113 placebo)
  - 131 emergent HIV-1 seroconversions were reported
    - 83 seroconversions occurred in subjects randomized to placebo
    - 48 seroconversions occurred in subjects in the emtricitabine and tenofovir DF for PrEP group
- 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

[†] The iPrEx Study was a randomized, double-blind, placebo-controlled, multinational clinical trial that included 2499 HIV-seronegative men or transgender women who have sex with men and with evidence of high-risk behaviour for HIV-1 infection. Subjects were randomly assigned to receive emtricitabine and tenofovir DF for PrEP (n=1251), or placebo (n=1248) once daily. Subjects received monthly HIV-1 testing, counseling, condoms, and management of other sexually transmitted infections. Duration of treatment was variable: subjects remained on treatment until the target number of seroconversion events was identified and the last enrolled study subject completed 48 weeks of treatment; subjects were followed for at least 8 weeks follow up; HBsAg reactive subjects were followed for hepatic flares for 24 weeks after study drug discontinuation; subjects who HIV-1 seroconverted during study were followed through at least 24 weeks after the last dose of study drugs. The primary outcome measure for the study was the incidence of documented HIV seroconversion.

The Partners PrEP Trial

- In another clinical trial of emtricitabine and tenofovir DF for a PrEP indication in serodiscordant couples, emtricitabine and tenofovir DF was shown to reduce HIV-1 infection acquisition by 75% for uninfected individuals exposed to the virus through heterosexual sex vs. placebo ($p<0.0001$)†
  - 95% Confidence Interval (55% to 87%)
  - 7827 person-years of follow up (2616 emtricitabine and tenofovir DF; 2604 VIREAD®; 2607 placebo)
  - 82 emergent HIV-1 seroconversions were reported
    - 52 seroconversions occurred in partner subjects randomized to placebo
    - 17 seroconversions occurred in partner subjects in the VIREAD group
    - 13 seroconversions occurred in partner subjects in the emtricitabine and tenofovir DF for PrEP group
- 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 Partners PrEP Study was a randomized, double-blind, placebo-controlled, 3-arm study that included 4758 HIV-serodiscordant heterosexual couples from Kenya and Uganda. Uninfected individuals were randomly assigned to receive emtricitabine and tenofovir DF for PrEP (n=1583), VIREAD†† (tenofovir disoproxil fumarate) (n=1589), or placebo (n=1586) once daily, with monthly follow-up for 24-36 months. All subjects received monthly HIV-1 testing, evaluation of adherence, assessment of sexual behavior, and safety evaluations

MINT-EMTRICITABINE/TENOFOVIR Safety Profile

IMPORTANT SAFETY INFORMATION

Contraindications

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

Warnings and Precautions Relating to the Use of MINT-EMTRICITABINE/ TENOFOVIR for a PrEP Indication

- **Comprehensive management to reduce the risk of acquiring HIV-1:** MINT-EMTRICITABINE/ TENOFOVIR 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 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)
  - Informing individuals about the importance of reducing sexually risky behaviors and supporting their efforts to do so
  - **Use MINT-EMTRICITABINE/TENOFOVIR to reduce the risk of acquiring HIV-1 only in individuals confirmed to be HIV-1 negative prior to initiating PrEP and re-confirmed routinely while taking PrEP.** HIV resistance substitutions may emerge with 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, 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 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 for HIV-1 infection at least once every 3 months while taking MINT-EMTRICITABINE/ TENOFOVIR for PrEP

- Evaluate for signs and symptoms of acute HIV-1 infection prior to prescribing and during treatment with MINT-EMTRICITABINE/TENOFOVIR 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 Health Canada 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 MINT-EMTRICITABINE/TENOFOVIR daily dosing schedule. 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 periodically 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. **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 PrEP, 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, or with drugs containing lamivudine, or with adefovir dipivoxil.

Important Safety Information

Common Adverse Events

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%.

Important Safety Information About the 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 and 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
- **Pediatrics:** The MINT-EMTRICITABINE/TENOFOVIR 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

Reminder about the use of MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication:

It is important to confirm and regularly reconfirm negative HIV-1 status before and while the individual is taking MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication.

- Confirm a negative 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 for HIV-1 infection at least once every 3 months while taking MINT-EMTRICITABINE/TENOFOVIR for PrEP
- It is important to be alert to the signs of potential acute HIV-1 infection when prescribing MINT-EMTRICITABINE/TENOFOVIR 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 Health Canada 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 MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication

Drug Interactions

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

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 correct and safe use of MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication.

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

For more information about MINT-EMTRICITABINE/TENOFOVIR and its indication for PrEP, please see the Product Monograph, including the BOXED WARNING and Consumer Information. You may also obtain additional information and educational materials about the use of MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication online at www.emtricitabine-tenofovir.com.

Post-Training Review Questions

1. **MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication should be used only:**
   a. As part of a comprehensive HIV-1 prevention strategy that includes other preventive measures since MINT-EMTRICITABINE/TENOFOVIR is not always effective in preventing the acquisition of HIV-1 infection
   b. In individuals who have been counseled to strictly adhere to their MINT-EMTRICITABINE/TENOFOVIR daily dosing schedule since the effectiveness of MINT-EMTRICITABINE/TENOFOVIR 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 MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication
   d. All of the above

2. **Which of the following statements is false?**
   a. MINT-EMTRICITABINE/TENOFOVIR should be used for a PrEP indication only in individuals confirmed to be HIV-1 negative
   b. MINT-EMTRICITABINE/TENOFOVIR has been found to be safe and effective for pre-exposure prophylaxis to reduce the risk of acquiring HIV-1 infection through injection drug use
   c. Women taking MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication should not breastfeed their babies
   d. MINT-EMTRICITABINE/TENOFOVIR for a PrEP indication 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 MINT-EMTRICITABINE/TENOFOVIR for 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 MINT-EMTRICITABINE/TENOFOVIR
   b. All people taking MINT-EMTRICITABINE/TENOFOVIR
   c. All people who discontinue MINT-EMTRICITABINE/TENOFOVIR
   d. None of the above

5. In clinical trials evaluating Emtricitabine and tenofovir DF for a PrEP indication, which of the following adverse reactions was not common?

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

6. MINT-EMTRICITABINE/TENOFOVIR 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 MINT-EMTRICITABINE/TENOFOVIR for 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 MINT-EMTRICITABINE/TENOFOVIR 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 MINT-EMTRICITABINE/TENOFOVIR 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

Indication and clinical use

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. When considering MINT-EMTRICITABINE/TENOFOVIR for PrEP, 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, 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

When prescribing MINT-EMTRICITABINE/TENOFOVIR for PrEP, healthcare providers must:

- 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 the recommended MINT-EMTRICITABINE/TENOFOVIR dosing schedule because 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;
- 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 one 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; and
- screen for HIV-1 infection at least once every 3 months while taking MINT-EMTRICITABINE/TENOFOVIR for PrEP.

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. Clinical studies of MINT-EMTRICITABINE/TENOFOVIR, EMTRIVA or VIREAD did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.
Safety and effectiveness in pediatric patients have not been established.

Contraindications

MINT-EMTRICITABINE/TENOFOVIR is contraindicated in patients with previously demonstrated hypersensitivity to any of the components of the product.

MINT-EMTRICITABINE/TENOFOVIR is contraindicated for use as PrEP in individuals with unknown or positive HIV- 1 status.

Most serious warnings and precautions

Lactic Acidosis and Severe Hepatomegaly with Steatosis: 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.

Post-Treatment Exacerbation of Hepatitis: 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 who are co-infected with HBV and HIV and 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 infected with HBV and discontinue MINT-EMTRICITABINE/TENOFOVIR. If appropriate, initiation of anti-hepatitis B therapy may be warranted.

Nephrotoxicity: 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.

Risk of Drug Resistance with Use of MINT-EMTRICITABINE/TENOFOVIR for Pre-Exposure Prophylaxis (PrEP) in Undiagnosed Early HIV-1 Infection: MINT-EMTRICITABINE/TENOFOVIR 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 Emtricitabine and tenofovir DF 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 infection are present unless negative infection status is confirmed.

Other relevant warnings and precautions

- Fat Redistribution
- Hepatic Impairment including severe or potentially fatal hepatic adverse events in patients with chronic hepatitis B or C
- Pancreatitis
- Bone Effects (Bone Mineral Density and Mineralization Defects)
- Renal Impairment
- Mothers should be instructed not to breast-feed if they are receiving MINT-EMTRICITABINE/TENOFOVIR
- Not recommended in pregnant women unless the potential benefit outweighs the potential risks to the fetus
- MINT-EMTRICITABINE/TENOFOVIR should not be administered with HEPSERA® (adefovir dipivoxil)
- Caution when used with HARVONI® particularly in those at risk of renal dysfunction

For More Information

Please consult the product monograph at www.mintpharmaceuticals.com for important information relating to adverse reactions, drug interactions, and dosing information which have not been discussed in this piece. The product monograph is also available by calling 1-877-398-9696.