EFAVIRENZ, EMTRICITABINE AND TENOFOVIR DISOPROXIL FUMARATE TABLETS

2023361

Rx only

## HIGHLIGHTS OF PRESCRIBING INFORMATION

**These highlights do not include all the information needed to use efavirenz, emtricitabine and tenofovir disoproxil fumarate safely and effectively. See full prescribing information for efavirenz, emtricitabine and tenofovir disoproxil fumarate.**

**EFAVIRENZ, EMTRICITABINE and TENOFOVIR Disoproxil Fumarate Tablets, for oral use**

**Initial U.S. Approval: 2006**

**WARNING: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS and POST TREATMENT EXACERBATION OF HEPATITIS B**

See full prescribing information for complete boxed warning.

- **Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including tenofovir disoproxil fumarate, a component of efavirenz, emtricitabine and tenofovir disoproxil fumarate. (5.1)**
- **Efavirenz, Emtricitabine and Tenofovir disoproxil fumarate is not approved for the treatment of chronic hepatitis B virus (HBV) infection and the safety and efficacy of efavirenz, emtricitabine and tenofovir disoproxil fumarate have not been established in patients coinfected with HBV and HIV-1. Severe acute exacerbations of hepatitis B have been reported in patients who have discontinued EMTRIVA or VIREAD, which are components of efavirenz, emtricitabine and tenofovir disoproxil fumarate. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who are coinfected with HIV-1 and HBV and if efavirenz, emtricitabine and tenofovir disoproxil fumarate is discontinued. If appropriate, initiation of anti-hepatitis B therapy may be warranted. *(See Warnings and Precautions (5.2)).***

**INDICATIONS AND USAGE**

Efavirenz, Emtricitabine and Tenofovir disoproxil fumarate tablet is indicated for use alone as a complete regimen or in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients 12 years of age and older. (1)

**DOSAGE AND ADMINISTRATION**

*Adults and pediatric patients 12 years of age and older with body weight at least 40 kg (at least 88 lbs):* The dose of efavirenz, emtricitabine and tenofovir disoproxil fumarate is one tablet once daily taken orally on an empty stomach. Dosing at bedtime may improve the tolerability of nervous system symptoms.

*Renal Impairment:* Because efavirenz, emtricitabine and tenofovir disoproxil fumarate tablet is a fixed-dose combination, it should not be prescribed for patients requiring dosage adjustment such as those with moderate or severe renal impairment (creatinine clearance below 50 mL/min).

*Rifampin Coadministration:* When efavirenz, emtricitabine and tenofovir disoproxil fumarate tablet is administered with rifampin to patients weighing 50 kg or more, an additional 200 mg dose of efavirenz is recommended *(See Drug Interactions (7.3), Table 4, and Clinical Pharmacology (12.3), Table 5).*

**DOSAGE FORMS AND STRENGTHS**

Efavirenz, Emtricitabine and Tenofovir disoproxil fumarate is available as tablets. Each tablet contains 600 mg of efavirenz, 200 mg of emtricitabine and 300 mg of tenofovir disoproxil fumarate (tenofovir DF, which is equivalent to 245 mg of tenofovir disoproxil). The tablets are pink colored, capsule shaped, film-coated tablets debossed with 'H' on one side and '128' on the other side

**CONTRAINDICATIONS**

- Previously demonstrated hypersensitivity (e.g., Stevens-Johnson syndrome, erythema multiforme, or toxic skin eruptions) to efavirenz, a component of efavirenz, emtricitabine and tenofovir disoproxil fumarate. (4.1)
- For some drugs, competition for CYP3A by efavirenz could result in inhibition of their metabolism and create the potential for serious and/or life-threatening adverse reactions (e.g., cardiac arrhythmias, prolonged sedation, or respiratory depression). (4.2)

**Revised: June 2013**

## FULL PRESCRIBING INFORMATION: CONTENTS*


**WARNING: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS and POST TREATMENT EXACERBATION OF HEPATITIS B**
**1 INDICATIONS AND USAGE**
**2 DOSAGE AND ADMINISTRATION**
**3 DOSAGE FORMS AND STRENGTHS**
**4 CONTRAINDICATIONS**
4.1 Hypersensitivity
4.2 Contraindicated Drugs
**5 WARNINGS AND PRECAUTIONS**
5.1 Lactic Acidosis/Severe Hepatomegaly with Steatosis
5.2 Patients Coinfected with HIV-1 and HBV
5.3 Drug Interactions
5.4 Coadministration with Related Products
5.5 Psychiatric Symptoms
5.6 Nervous System Symptoms
5.7 New Onset or Worsening Renal Impairment
5.8 Reproductive Risk Potential
5.9 Rash
5.10 Hepatotoxicity
5.11 Decreases in Bone Mineral Density
5.12 Convulsions
5.13 Immune Reconstitution Syndrome
5.14 Fat Redistribution
**6 ADVERSE REACTIONS**
6.1 Adverse Reactions from Clinical Trials Experience
6.2 Laboratory Abnormalities
6.3 Postmarketing Experience
**7 DRUG INTERACTIONS**
7.1 Efavirenz
7.2 Emtricitabine and Tenofovir Disoproxil Fumarate
7.3 Efavirenz, Emtricitabine and Tenofovir Disoproxil Fumarate
7.4 Efavirenz Assay Interference
**8 USE IN SPECIFIC POPULATIONS**
8.1 Pregnancy
8.3 Nursing Mothers
8.4 Pediatric Use
8.5 Geriatric Use
8.6 Hepatic Impairment
8.7 Renal Impairment
**10 OVERDOSAGE**
**11 DESCRIPTION**
**12 CLINICAL PHARMACOLOGY**
12.1 Mechanism of Action
12.3 Pharmacokinetics
12.4 Microbiology
**13 NONCLINICAL TOXICOLOGY**
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
13.2 Animal Toxicology and/or Pharmacology
**14 CLINICAL STUDIES**
**16 HOW SUPPLIED/STORAGE AND HANDLING**
**17 PATIENT COUNSELING INFORMATION**
17.1 Drug Interactions
17.2 General Information for Patients
17.3 Lactic Acidosis/Severe Hepatomegaly with Steatosis
17.4 Patients Co-infected with HIV-1 and HBV
17.5 New Onset or Worsening Renal Impairment
17.6 Decreases in Bone Mineral Density
17.7 Dosing Instructions
17.8 Nervous System Symptoms
17.9 Psychiatric Symptoms
17.10 Rash
17.11 Reproductive Risk Potential


* Sections or subsections omitted from the full prescribing information are not listed

## FULL PRESCRIBING INFORMATION

**WARNINGS: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS and POST TREATMENT EXACERBATION OF HEPATITIS B**

**Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including tenofovir disoproxil fumarate, a component of efavirenz, emtricitabine and tenofovir disoproxil fumarate, in combination with other antiretrovirals *(See Warnings and Precautions (5.1)).***

**Efavirenz, Emtricitabine and Tenofovir disoproxil fumarate is not approved for the treatment of chronic hepatitis B virus (HBV) infection and the safety and efficacy of efavirenz, emtricitabine and tenofovir disoproxil fumarate have not been established in patients coinfected with HBV and HIV-1. Severe acute exacerbations of hepatitis B have been reported in patients who have discontinued EMTRIVA or VIREAD, which are components of efavirenz, emtricitabine and tenofovir disoproxil fumarate. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who are coinfected with HIV-1 and HBV and if efavirenz, emtricitabine and tenofovir disoproxil fumarate is discontinued. If appropriate, initiation of anti-hepatitis B therapy may be warranted *(See Warnings and Precautions (5.2)).***

**INDICATIONS AND USAGE**

Efavirenz, Emtricitabine and Tenofovir disoproxil fumarate tablet is indicated for use alone as a complete regimen or in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients 12 years of age and older.

**DOSAGE AND ADMINISTRATION**

*Adults and pediatric patients 12 years of age and older with body weight at least 40 kg (at least 88 lbs):* The dose of efavirenz, emtricitabine and tenofovir disoproxil fumarate is one tablet once daily taken orally on an empty stomach. Dosing at bedtime may improve the tolerability of nervous system symptoms.

*Renal Impairment:* Because efavirenz, emtricitabine and tenofovir disoproxil fumarate tablet is a fixed-dose combination, it should not be prescribed for patients requiring dosage adjustment such as those with moderate or severe renal impairment (creatinine clearance below 50 mL/min).

*Rifampin Coadministration:* When efavirenz, emtricitabine and tenofovir disoproxil fumarate tablet is administered with rifampin to patients weighing 50 kg or more, an additional 200 mg dose of efavirenz is recommended *(See Drug Interactions (7.3), Table 4, and Clinical Pharmacology (12.3), Table 5).*

**DOSAGE FORMS AND STRENGTHS**

Efavirenz, Emtricitabine and Tenofovir disoproxil fumarate is available as tablets. Each tablet contains 600 mg of efavirenz, 200 mg of emtricitabine and 300 mg of tenofovir disoproxil fumarate (tenofovir DF, which is equivalent to 245 mg of tenofovir disoproxil). The tablets are pink colored, capsule shaped, film-coated tablets debossed with 'H' on one side and '128' on the other side

**CONTRAINDICATIONS**

- Previously demonstrated hypersensitivity (e.g., Stevens-Johnson syndrome, erythema multiforme, or toxic skin eruptions) to efavirenz, a component of efavirenz, emtricitabine and tenofovir disoproxil fumarate. (4.1)
- For some drugs, competition for CYP3A by efavirenz could result in inhibition of their metabolism and create the potential for serious and/or life-threatening adverse reactions (e.g., cardiac arrhythmias, prolonged sedation, or respiratory depression). (4.2)

**WARNINGS AND PRECAUTIONS**

- Serious psychiatric symptoms: Immediate medical evaluation is recommended. (5.5, 6.1)
- Nervous system symptoms (NSS): NSS are frequent, usually begin 1 to 2 days after initiating therapy and resolve in 2 to 4 weeks. Dosing at bedtime may improve tolerability. NSS are not predictive of onset of psychiatric symptoms. (2,5.6)
- New onset or worsening renal impairment: Can include acute renal failure and Fanconi syndrome. Assess creatinine clearance (CrCl) before initiating treatment with efavirenz, emtricitabine and tenofovir disoproxil fumarate. Monitor CrCl and serum phosphorus in patients at risk. Avoid administering efavirenz, emtricitabine and tenofovir disoproxil fumarate with concurrent or recent use of nephrotoxic drugs. (5.7)
- Pregnancy: Fetal harm can occur when administered to a pregnant woman during the first trimester. Women should be apprised of the potential harm to the fetus. A pregnancy registry is available. (5.8, 8.1)
- Rash: Discontinue if severe rash develops. (5.9, 6.1)
- Hepatotoxicity: Monitor liver function tests before and during treatment in patients with underlying hepatic disease, including hepatitis B or C coinfection, marked transaminase elevations, or who are taking medications associated with liver toxicity. Among reported cases of hepatic failure, a few occurred in patients with no pre-existing hepatic disease. (5.10, 6.3, 8.6)
- Decreases in bone mineral density (BMD): Consider assessment of BMD in patients with a history of pathological fracture or other risk factors for osteoporosis or bone loss. (5.11)
- Convulsions: Use caution in patients with a history of seizures. (5.12)
- Immune reconstitution syndrome: May necessitate further evaluation and treatment. (5.13)
- Redistribution/accumulation of body fat: Observed in patients receiving antiretroviral therapy. (5.14)
- Coadministration with other products: Do not use with drugs containing emtricitabine or tenofovir disoproxil fumarate including COMPLERA, EMTRIVA, STRIBILD, TRUVADA, or VIREAD, or with drugs containing lamivudine. SUSTIVA (efavirenz) should not be coadministered with efavirenz, emtricitabine and tenofovir disoproxil fumarate unless required for dose-adjustment when coadministered with rifampin. (5.4) Do not administer in combination with HEPSERA. (5.2)

**ADVERSE REACTIONS**

Most common adverse reactions (incidence greater than or equal to 10%) observed in an active-controlled clinical trial of efavirenz, emtricitabine, and tenofovir DF are diarrhea, nausea, fatigue, headache, dizziness, depression, insomnia, abnormal dreams, and rash. (6)

**To report SUSPECTED ADVERSE REACTIONS, contact Hetero Labs Limited at 866-495-1995 or FDA at 1-800-FDA-1088 or** www.fda.gov/medwatch

**DRUG INTERACTIONS**

- Efavirenz: Coadministration of efavirenz can alter the concentrations of other drugs and other drugs may alter the concentrations of efavirenz. The potential for drug-drug interactions must be considered before and during therapy. (4.2, 7.1, 12.3)
- Didanosine: Tenofovir disoproxil fumarate increases didanosine concentrations. Use with caution and monitor for evidence of didanosine toxicity (e.g., pancreatitis, neuropathy) when co administered. Consider dose reductions or discontinuations of didanosine if warranted. (7.2)
- Atazanavir: Coadministration of efavirenz, emtricitabine and tenofovir disoproxil fumarate and atazanavir or atazanavir/ritonavir is not recommended. (7.3)
- Lopinavir/ritonavir: Coadministration increases tenofovir concentrations Monitor for evidence of tenofovir toxicity. (7.3)

**USE IN SPECIFIC POPULATIONS**

- Pregnancy: Women should avoid pregnancy while receiving efavirenz, emtricitabine and tenofovir disoproxil fumarate and for 12 weeks after discontinuation of efavirenz. (8.1)
- Nursing mothers: Women infected with HIV should be instructed not to breastfeed. (8.3)
- Hepatic impairment: Efavirenz, Emtricitabine and Tenofovir disoproxil fumarate is not recommended for patients with moderate or severe hepatic impairment. Use caution in patients with mild hepatic impairment. (8.10, 8.6)
- Pediatrics: The incidence of rash was higher than in adults. (5.9, 6.1)

**See 17 for PATIENT COUNSELING INFORMATION and FDA approved patient labeling.**

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7.4 Efavirenz Assay Interference
**8 USE IN SPECIFIC POPULATIONS**
8.1 Pregnancy
8.3 Nursing Mothers
8.4 Pediatric Use
8.5 Geriatric Use
8.6 Hepatic Impairment
8.7 Renal Impairment
**10 OVERDOSAGE**
**11 DESCRIPTION**
**12 CLINICAL PHARMACOLOGY**
12.1 Mechanism of Action
12.3 Pharmacokinetics
12.4 Microbiology
**13 NONCLINICAL TOXICOLOGY**
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
13.2 Animal Toxicology and/or Pharmacology
**14 CLINICAL STUDIES**
**16 HOW SUPPLIED/STORAGE AND HANDLING**
**17 PATIENT COUNSELING INFORMATION**
17.1 Drug Interactions
17.2 General Information for Patients
17.3 Lactic Acidosis/Severe Hepatomegaly with Steatosis
17.4 Patients Co-infected with HIV-1 and HBV
17.5 New Onset or Worsening Renal Impairment
17.6 Decreases in Bone Mineral Density
17.7 Dosing Instructions
17.8 Nervous System Symptoms
17.9 Psychiatric Symptoms
17.10 Rash
17.11 Reproductive Risk Potential


* Sections or subsections omitted from the full prescribing information are not listed

## 1 INDICATIONS AND USAGE

Efavirenz, Emtricitabine and Tenofovir disoproxil fumarate tablet, a combination of 2 nucleoside analog HIV-1 reverse transcriptase inhibitors and 1 non-nucleoside HIV-1 reverse transcriptase inhibitor, is indicated for use alone as a complete regimen or in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients 12 years of age and older. (1)

## 2 DOSAGE AND ADMINISTRATION

- Recommended dose in adults and pediatric patients (12 years of age and older and weighing at least 40 kg): One tablet once daily taken orally on an empty stomach, preferably at bedtime. (2)
- Dose in renal impairment: Should not be administered in patients with creatinine clearance below 50 mL/min. (2)
- With rifampin coadministration, an additional 200 mg/day of efavirenz is recommended for patients weighing 50 kg or more. (2)

## 3 DOSAGE FORMS AND STRENGTHS

Tablet containing 600 mg of efavirenz, 200 mg of emtricitabine and 300 mg of tenofovir disoproxil fumarate. (3)

## 4 CONTRAINDICATIONS

- Previously demonstrated hypersensitivity (e.g., Stevens-Johnson syndrome, erythema multiforme, or toxic skin eruptions) to efavirenz, a component of efavirenz, emtricitabine and tenofovir disoproxil fumarate. (4.1)
- For some drugs, competition for CYP3A by efavirenz could result in inhibition of their metabolism and create the potential for serious and/or life-threatening adverse reactions (e.g., cardiac arrhythmias, prolonged sedation, or respiratory depression). (4.2)

## 5 WARNINGS AND PRECAUTIONS

### 5.1 Lactic Acidosis /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, a component of efavirenz, emtricitabine and tenofovir disoproxil fumarate in combination with other antiretrovirals. A majority of these cases have been in women. Obesity and prolonged nucleoside exposure may be risk factors. Particular caution should be exercised when administering nucleoside analogs to any patient with known risk factors for liver disease; however, cases have also been reported in patients with no known risk factors. Treatment with efavirenz, emtricitabine and tenofovir disoproxil fumarate should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked transaminase elevations).

### 5.2 Patients Coinfected with HIV-1 and HBV

It is recommended that all patients with HIV-1 be tested for the presence of chronic HBV before initiating antiretroviral therapy. Efavirenz, Emtricitabine and Tenofovir disoproxil fumarate is not approved for the treatment of chronic HBV infection, and the safety and efficacy of efavirenz, emtricitabine and tenofovir disoproxil fumarate have not been established in patients coinfected with HBV and HIV-1. Severe acute exacerbations of hepatitis B have been reported in patients who are coinfected with HBV and HIV-1 and have discontinued emtricitabine or tenofovir DF, two of the components of efavirenz, emtricitabine and tenofovir disoproxil fumarate. In some patients infected with HBV and treated with emtricitabine, severe acute exacerbations of hepatitis B were associated with liver decompensation and liver failure. Patients who are coinfected with HIV-1 and HBV should be closely monitored with both clinical and laboratory follow up for at least several months after stopping treatment with efavirenz, emtricitabine and tenofovir disoproxil fumarate. If appropriate, initiation of anti-hepatitis B therapy may be warranted.

Efavirenz, Emtricitabine and Tenofovir disoproxil fumarate should not be administered with HEPSERA[®] (adefovir dipivoxil). It is also important to tell your healthcare provider if you are taking any of the following:

- Fortovase, Invirase (saquinavir), Biaxin (clarithromycin), Noxafil (Posaconazole), Sporanox (itraconazole), or Victrelis (boceprevir); **these medicines may need to be replaced with another medicine when taken with efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets.**
- Calcium channel blockers such as Cardizem or Tiazac (diltiazem), Covera HS or Isoptin (verapamil) and others; Crixivan (indinavir), Selzentry (maraviroc); the immunosuppressant medicines cyclosporine (Gengraf, Neoral, Sandimmune, and others), Prograf (tacrolimus), or Rapamune (sirolimus); Methadone; Mycobutin (rifabutin); Rifampin; cholesterol-lowering medicines such as Lipitor (atorvastatin), Pravachol (pravastatin sodium), and Zocor (simvastatin); Viracept (nelfinavir); Wellbutrin (bupropion, oxidopamine, hydroxybupropion, Wellbutrin SR, Wellbutrin XL, and Zyban) or Zoloft (sertraline); **dose changes may be needed when these drugs are taken with efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets.**
- Videx, Videx EC (didanosine); tenofovir DF (a component of efavirenz, emtricitabine and tenofovir disoproxil fumarate) tablets may increase the amount of didanosine in your blood, which could result in more side effects. **You may need to be monitored more carefully** if you are taking efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets and didanosine together. Also, the dose of didanosine may need to be changed.
- Reyataz (atazanavir sulfate) or Kaletra (lopinavir/ ritonavir); these medicines may increase the amount of tenofovir DF (a component of Efavirenz, Emtricitabine and Tenofovir disoproxil fumarate) in your blood, which could result in more side effects. Reyataz is not recommended with efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets. **You may need to be monitored more carefully** if you are taking efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets and Kaletra together. Also, the dose of Kaletra may need to be changed.
- Medicine for seizures [for example, Dilantin (phenytoin), Tegretol (carbamazepine) or phenobarbital]; your healthcare provider may want to switch you to another medicine or check the levels in your blood from time to time.

**These are not all the medicines that may cause problems if you take efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets. Be sure to tell your healthcare provider about all medicines that you take.**

Keep a complete list of all the prescription and nonprescription medicines as well as any herbal remedies that you are taking, how much you take, and how often you take them. Make a new list when medicines or herbal remedies are added or stopped, or if the dose changes. Give copies of this list to all of your healthcare providers and pharmacists **every** time you visit your healthcare provider or fill a prescription. This will give your healthcare provider a complete picture of the medicines you use. Then he or she can decide the best approach for your situation.

**How should I take efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets?**

- Take the exact amount of efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets your healthcare provider prescribes. Never change the dose on your own. Do not stop this medicine unless your healthcare provider tells you to stop.
- You should take efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets on an empty stomach.
- Swallow efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets with water.
- Taking efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets at bedtime may make some side effects less bothersome.
- Do not miss a dose of efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets. If you forget to take efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets, take the missed dose right away, unless it is almost time for your next dose. Do not double the next dose. Carry on with your regular dosing schedule. If you need help in planning the best times to take your medicine, ask your healthcare provider or pharmacist.
- If you believe you took more than the prescribed amount of efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets, contact your local poison control center or emergency room right away.
- Tell your healthcare provider if you start any new medicine or change how you take old ones. Treatment with efavirenz may affect other medicines.
- When your efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets supply starts to run low, get more from your healthcare provider or pharmacy. This is very important because the amount of virus in your blood may increase if the medicine is stopped for even a short time. The virus may develop resistance to efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets and become harder to treat.

Your healthcare provider may want to check your blood tests to check for certain side effects while you take efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets.

**What should I avoid while taking efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets?**

- **Do not become pregnant while taking efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets and for 12 weeks after stopping it.** Serious birth defects have been seen in the babies of animals and women treated with efavirenz (a component of efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets) during pregnancy. It is not known if another efavirenz caused these birth defects. **Tell your healthcare provider right away if you are pregnant.** Also talk with your healthcare provider if you want to become pregnant.
- Women should not rely only on hormone-based birth control, such as pills, injections, or implants, because efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets may make these contraceptives ineffective. Women must use a reliable form of barrier contraception, such as a condom or diaphragm, even if they also use other methods of birth control. Efavirenz, a component of efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets, may remain in your blood for a time after therapy is stopped. Therefore, you should continue to use contraceptive measures for 12 weeks after you stop taking efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets.
- **Do not breastfeed.** Some of the medicines in efavirenz, emtricitabine and tenofovir disoproxil fumarate can be passed to your baby in your breast milk. We do not know whether it could harm your baby. Also, mothers with HIV-1 should not breastfeed because HIV-1 can be passed to the baby in the breast milk.
- Taking efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets with alcohol or medicines containing alcohol may increase side effects as efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets, such as drowsiness, may increase those side effects.
- Avoid doing things that can spread HIV-1 to others.
  - **Do not share needles or other injection equipment.**
  - **Do not share personal items that can have blood or body fluids on them, like toothbrushes and razor blades.**
  - **Do not have any kind of sex without protection.** Always practice safe sex by using a latex or polyurethane condom to lower the chance of sexual contact with semen, vaginal secretions, or blood. Even if you take efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets, or any other safe sex practice, you can still spread HIV-1 to others.

**What are the possible side effects of efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets?**

**Efavirenz, Emtricitabine and Tenofovir disoproxil fumarate tablets may cause the following serious side effects:**

- **Lactic acidosis** (buildup of an acid in the blood). Lactic acidosis can be a medical emergency and may need to be treated in the hospital. **Call your healthcare provider right away if you get signs of lactic acidosis.** See "What is the most important information I should know about emtricitabine and tenofovir disoproxil fumarate tablets?".
- **Serious liver problems (hepatotoxicity)**, with liver enlargement (hepatomegaly) and fat in the liver (steatosis). Call your healthcare provider right away if you get signs of liver problems. See "What is the most important information I should know about efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets?".
- **"Flare-ups" of Hepatitis B Virus (HBV) infection**, in which the disease suddenly returns in a worse way than before, can occur if you have HBV and you stop taking efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets. Your healthcare provider will monitor your condition for several months after stopping efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets if you have both HIV-1 and HBV infection and may recommend treatment for your HBV. Efavirenz, Emtricitabine and Tenofovir disoproxil fumarate tablets are not approved for the treatment of hepatitis B virus infection. If you have advanced liver disease and stop treatment with efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets, the "flare-up" can be more severe. Tell your healthcare provider if you have any new or worsening symptoms of hepatitis B.
- **Serious psychiatric problems.** A small number of patients may experience severe depression, strange thoughts, or angry behavior while taking efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets. Some patients have thoughts of suicide and a few have actually committed suicide. These problems may occur more often in patients who have had mental illness. Contact your healthcare provider right away if you think you are having these psychiatric symptoms, so your healthcare provider can decide if you should continue to take efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets.
- **Kidney problems** (including decline or failure of kidney function). If you have had kidney problems in the past or take other medicines that can cause kidney problems, your healthcare provider should do regular blood tests to check your kidneys. Symptoms that may be related to kidney problems include a high volume of urine, thirst, muscle pain, and muscle weakness.
- **Other serious liver problems.** Some patients have experienced serious liver problems including liver failure resulting in transplantation or death. Most of these serious side effects occurred in patients with a chronic liver disease such as hepatitis infection, or cirrhosis, but there have also been a few reports in patients without any existing liver disease.
- **Changes in bone mineral density (weakened bones).** Laboratory tests show changes in the bones of patients treated with tenofovir DF, a component of efavirenz, emtricitabine and tenofovir disoproxil fumarate. Some HIV patients treated with tenofovir DF developed thinning of the bones (osteopenia) which could lead to fractures. If you have had bone problems in the past, your healthcare provider may need to do tests to check your bone mineral density or may prescribe medicines to help your bone mineral density. Additionally, bone pain and softening of the bone (which may contribute to fractures) may occur as a consequence of kidney problems.

**Common side effects:**

Patients may have dizziness, headache, trouble sleeping, drowsiness, trouble concentrating, and/or unusual dreams during treatment with efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets. These side effects may be reduced if you take efavirenz, emtricitabine and tenofovir disoproxil fumarate at bedtime on an empty stomach. They also tend to go away after you have taken the medicine for a few weeks. If you have these common side effects, such as dizziness, it does not mean that you will also have more psychiatric problems, such as severe depression, strange thoughts, or angry behavior. Tell your healthcare provider right away if any of these side effects continue or if they bother you. It is possible that these symptoms may be more severe if efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets are used with alcohol or mood altering (street) drugs.

If you are dizzy, have trouble concentrating, or are drowsy, avoid activities that may be dangerous, such as driving or operating machinery.

Rash may be common. Rashes usually go away without any change in treatment. In a small number of patients, rash may be serious. If you develop a rash, call your healthcare provider right away. **Rash may be a serious problem in some children**. Tell your child's healthcare provider right away if you notice rash on any other side effects. Tell your healthcare provider right away if any other side effects continue or if they bother you. It is possible that these symptoms may be more severe if efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets are used with alcohol or mood altering (street) drugs.

**Other possible side effects with efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets:**

- Changes in body fat. Changes in body fat develop in some patients taking anti HIV-1 medicines. These changes may include an increased amount of fat in the upper back and neck ("buffalo hump"), in the breasts, and around the trunk. Loss of fat from the legs, arms, and face may also happen. The cause and long-term health effects of these fat changes are not known.
- Skin discoloration (small spots or freckles) may also happen with efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets.
- In some patients with advanced HIV infection (AIDS), signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is started. It is believed that these symptoms are due to an improvement in the body's immune response, enabling the body to fight infections that may have been present with no obvious symptoms. If you notice any symptoms of infection, please inform your doctor immediately.
- Additional side effects are inflammation of the pancreas, allergic reaction (including swelling of the face, lips, tongue, or throat), shortness of breath, pain, stomach pain, weakness and indigestion.

Tell your healthcare provider or pharmacist if you notice any side effects while taking efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets.

Contact your healthcare provider before stopping efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets because of side effects or for any other reason.

This is not a complete list of side effects possible with efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets. Ask your healthcare provider or pharmacist for a more complete list of side effects of efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets and all the medicines you will take

**How do I store efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets ?**

- **Keep efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets and all other medicines out of reach of children.**
- Store efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets below 30°C, protect from moisture
- Keep efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets in its original container and keep the container tightly closed.
- Do not keep medicine that is out of date or that you no longer need. If you throw any medicines away make sure that children will not find them.

**General information about efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets:**

Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not use efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets for a condition for which it was not prescribed. Do not give efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets to other people, even if they have the same symptoms you have. It may harm them.

This leaflet summarizes the most important information about efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets that is written for health professionals.

Do not use efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets if the seal over bottle opening is broken or missing.

**What are the ingredients of efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets?**

**Active Ingredients:** efavirenz, emtricitabine, and tenofovir disoproxil fumarate

**Inactive Ingredients:** croscarmellose sodium, hydroxypropyl cellulose, magnesium stearate, microcrystalline cellulose and sodium lauryl sulfate. The tablets are coated with opadry II pink containing black iron oxide, polyethylene glycol, polyvinyl alcohol, red iron oxide, talc, and titanium dioxide.

**June 2013**

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Manufactured by:
**HETERO LABS LIMITED**
Unit-V, Polepally, Jadcherla,
Mahaboob Nagar-509 301, India.

## Patient Information

**Efavirenz, Emtricitabine and Tenofovir disoproxil fumarate Tablets**
**ALERT: Find out about medicines that should NOT be taken with efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets.**

Please also read the section **"MEDICINES YOU SHOULD NOT TAKE WITH EFAVIRENZ, EMTRICITABINE AND TENOFOVIR DISOPROXIL FUMARATE TABLETS.**

Generic name: efavirenz, emtricitabine and tenofovir disoproxil fumarate (eh FAH vih renz, em tri SIT uh bean and te NOE' fo veer dye soe PROX il FYOU marate)

Read the Patient Information that comes with efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets before you start taking it and each time you get a refill since there may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment. You should stay under a healthcare provider's care when taking efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets. **Do not change or stop your medicine without first talking with your healthcare provider**. Talk to your healthcare provider or pharmacist if you have any questions about efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets.

**What is the most important information I should know about efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets?**

**Some people who have taken medicine like efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets (which contains nucleoside analogs) have developed a serious condition called lactic acidosis** (build up of an acid in the blood). Lactic acidosis can be a medical emergency and may need to be treated in the hospital. **Call your healthcare provider right away if you get the following signs or symptoms of lactic acidosis:**

- You feel very weak or tired.
- You have unusual (not normal) muscle pain.
- You have trouble breathing.
- You have stomach pain with nausea and vomiting.
- You feel cold, especially in your arms and legs.
- You feel dizzy or lightheaded.
- You have a fast or irregular heartbeat.
- **Some people who have taken medicines like efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets have developed serious liver problems called hepatotoxicity**, with liver enlargement (hepatomegaly) and fat in the liver (steatosis). **Call your healthcare provider right away if you get the following signs or symptoms of liver problems:**

- Your skin or the white part of your eyes turns yellow (jaundice).
- Your urine turns dark.
- Your bowel movements (stools) turn light in color.
- You don't feel like eating food for several days or longer.
- You feel sick to your stomach (nausea).
- You have lower stomach area (abdominal) pain.
- **You may be more likely to get lactic acidosis or liver problems** if you are female, very overweight (obese), or have been taking nucleoside analog-containing medicines, like efavirenz, emtricitabine and tenofovir disoproxil fumarate, for a long time.
- **If you also have hepatitis B Virus (HBV) infection and you stop taking efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets you may get a "flare-up" of your hepatitis. A "flare-up" is when the disease suddenly returns in a worse way than before.** Patients with HBV who stop taking efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets need close medical follow-up for several months, including medical exams and blood tests to check for hepatitis that could be getting worse .Efavirenz, Emtricitabine and Tenofovir disoproxil fumarate tablets are not approved for the treatment of HBV, so you must discuss your HBV therapy with your healthcare provider.

**What are efavirenz, emtricitabine and tenofovir disoproxil fumarate tablets?**

Efavirenz, Emtricitabine and Tenofovir disoproxil fumarate tablets contains 3 medicines, SUSTIVA® (efavirenz), EMTRIVA® (emtricitabine) and VIREAD® (tenofovir