

PRESCRIBING INFORMATION

Tenofovir Disoproxil Fumarate, Lamivudine & Efavirenz Tablets

TUDOBEST-LE™

GENERIC NAME:

Tenofovir Disoproxil Fumarate, Lamivudine & Efavirenz Tablets.

COMPOSITION:

Each Film coated tablet contains:

Tenofovir Disoproxil Fumarate300mg
Lamivudine300mg
Efavirenz600mg
Colours: Titanium dioxide & Indigo carmine

DETAILED PHARMACOLOGY

Efavirenz:

Efavirenz is a non-nucleoside reverse transcriptase (RT) inhibitor of human immunodeficiency virus type 1 (HIV-1). Efavirenz is predominantly a non-competitive inhibitor of HIV-1 RT. HIV-2 RT and human cellular DNA polymerases α , β , γ , and δ are not inhibited by efavirenz.

Lamivudine:

Lamivudine is phosphorylated to its active 5'-triphosphate metabolite, Lamivudine triphosphate (3TC-TP). The principal mode of action of 3TC-TP is the inhibition of HIV-1 reverse transcriptase (RT) via DNA chain termination after incorporation of the nucleotide analogue into viral DNA. 3TC-TP is a weak inhibitor of mammalian DNA polymerases α , β , and γ .

Tenofovir DF:

Tenofovir DF is an acyclic nucleoside phosphonate diester analog of adenosine monophosphate. Tenofovir DF 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. Tenofovir diphosphate is a weak inhibitor of mammalian DNA polymerases α , β , and mitochondrial DNA polymerase γ .

Resistance

Efavirenz:

HIV-1 isolates with reduced susceptibility to efavirenz (>380-fold increase in EC90) compared to baseline emerged rapidly under selection in cell culture in the presence of drug.

Genotypic characterization of these viruses identified mutations resulting in single amino acid substitutions L100I or V179D, double substitutions L100I/V108I and triple substitutions L100I/V179D/Y181C in RT. Other resistance mutations observed to emerge commonly included L100I (7%), K101E/Q/R (14%), V108I (11%), G190S/T/A (7%), P225H (18%), and M230I/L (11%).

Phenotypic (N=26) changes in evaluable HIV-1 isolates and genotypic (N=104) changes in plasma virus from selected patients treated with efavirenz in combination with indinavir, or with zidovudine plus lamivudine, were monitored. Clinical isolates with reduced susceptibility in vitro to efavirenz have been obtained. One or more RT mutations at amino acid positions 98, 100, 101, 103, 106, 108, 188, 190 and 225, and 227 were observed in all 102 of 104 patients with a frequency of at least 9% compared to baseline. **Lamivudine:**

Lamivudine-resistant variants of HIV-1 have been selected in cell culture. Genotypic analysis showed that the resistance was due to a specific amino acid substitution in the HIV-1 reverse transcriptase at codon 184 changing the methionine to either isoleucine or valine (M184V/I)

Tenofovir DF:

HIV-1 isolates with reduced susceptibility to tenofovir have been selected in vitro. These viruses expressed a K65R mutation in RT and showed a 2–4-fold reduction in susceptibility to tenofovir.

Cross-resistance

Efavirenz:

Rapid emergence of HIV-1 strains that are cross-resistant to non-nucleoside RT inhibitors has been observed in vitro. Thirteen clinical isolates previously characterized as efavirenz resistant were also phenotypically resistant to nevirapine and delavirdine in vitro compared to baseline. Clinically derived zidovudine-resistant HIV-1 isolates tested in vitro retained susceptibility to efavirenz. Cross-resistance between efavirenz and HIV protease inhibitors is unlikely because of the different enzyme targets involved.

Lamivudine: Many new copies of HIV are mutations. They are slightly different from the original virus. Some mutations can keep multiplying even when you are taking an ARV. When this happens, the drug will stop working. This is called "developing resistance" to the drug. Sometimes, if your virus develops resistance to one drug, it will also have resistance to other ARVs. This is called "cross-resistance." Resistance can develop quickly. It is very important to take ARVs according to instructions, on schedule, and not to skip or reduce doses. Lamivudine seems to be able to reduce resistance to AZT. After people develop resistance to AZT and then take lamivudine, AZT seems to work better for them.

Tenofovir D/F:

The K65R mutation selected by tenofovir is also selected in some HIV-1 infected patients treated with abacavir, didanosine, or zalcitabine. HIV-1 isolates with the K65R mutation also showed reduced susceptibility to emtricitabine and lamivudine. Therefore, cross-resistance among these drugs may occur in patients whose virus harbors the K65R mutation. HIV-1 isolates from patients (N=20) whose HIV-1 expressed a mean of 3 zidovudine associated RT amino acid substitutions (M41L, D67N, K70R, L210W, T215Y/F, or K219Q/E/N) showed a 3.1-fold decrease in the susceptibility to tenofovir. Multinucleoside resistant HIV-1 with a T69S double insertion mutation in the RT showed reduced susceptibility to tenofovir.

DO NOT TAKE TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET IF:

Tenofovir DF, a component of TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET, caused harm to the bones of animals. If you notice bone pain, suffer a bone fracture, or other bone problem, consult your doctor. If you have bone problems, you may wish to discuss calcium and/or vitamin D supplementation with your doctor. The effect of supplementation with calcium and/or vitamin D is unknown.

BEFORE YOU USE TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET TALK TO YOUR DOCTOR OR PHARMACIST:

If you have ever had a previous life threatening skin reaction (e.g. Stevens-Johnson syndrome).

If you are breast-feeding or plan to breast-feed: Do not breast-feed if you have HIV or are taking TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET. HIV can be passed to your baby in your breast milk. The component of TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET, tenofovir DF, can be passed to your baby in your breast milk and may cause harm to your baby. Talk to your doctor about the best way to feed your baby.

INTERACTIONS WITH THIS MEDICATION

Drugs that must not be taken with TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET:

Propulsid (cisapride)*, Versed (midazolam), Halcion (triazolam), ergot medications (for example Wigraine and Cafergot), Hismanal (astemizole)*, Seldane (terfenadine)*, Vascor (bepridil)* or Orap (pimozide). Taking these medications with TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET could create the potential for serious or life-threatening side effects.

Vfend (voriconazole) since it may lose its effect or may increase the chance of having side effects from TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET.

Do not take TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET if you are taking St. John's wort (Hypericum perforatum), or products containing St. John's wort. St. John's wort is an herbal product sold as a dietary supplement. Taking St. John's wort may decrease TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET levels and may lead to increased viral load and possible resistance to efavirenz or resistance to the class of nonnucleoside reverse transcriptase inhibitors (NNRTIs).

Do not take TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET if you are taking emtricitabine because these drugs are very similar and there is no additional benefit. Blood levels of lamivudine may be increased by bactrim or septria.

It is also important to tell your doctor if you are taking any of the following:

Do not take TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET if you are on other medications that may affect your kidneys and have not discussed this with your doctor.

Reyataz (atazanavir sulfate), Fortovase or Invirase (saquinavir), or Biaxin (clarithromycin); these medicines need to be replaced with another medicine when taken with TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET. If your doctor does prescribe Reyataz and TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET together, you may need to be monitored more carefully for side effects.

Celsentri (maraviroc)

Crixivan (indinavir), methadone, Mycobutin (rifabutin), Zolof (sertraline), Wellbutrin SR, Wellbutrin XL, or Zyban (bupropion); these medicines may need to have their dose changed when taken with TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET.

Videx or Videx EC (didanosine); Tenofovir DF (a component of TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET) 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 TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET and didanosine together. Also, the dose of didanosine may need to be changed.

PROPER USE OF THIS MEDICATION

Stay under a doctor's care when taking TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET. Do not change your treatment or stop treatment without first talking with your doctor.

Take TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET exactly as your doctor prescribed it. Follow the directions from your doctor, exactly as written on the label. Set up a dosing schedule and follow it carefully.

When your TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET supply starts to run low, get more from your doctor 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 TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET and become harder to treat.

Only take medicine that has been prescribed specifically for you. Do not give TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET to others or take medicine prescribed for someone else.

Do not use if seal over botTenofovir Disoproxil Fumarate, Lamivudine & Efavirenz opening is broken or missing.

Usual Adult Dose:

The usual dose of TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET is one tablet orally (by mouth) once a day, in combination with other anti-HIV medicines.

TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET may be taken with or without a meal.

Over dosage:

In case of drug overdose, contact a healthcare practitioner, hospital emergency department or regional poison control centre, even if there are no symptoms.

Missed Dose:

It is important that you do not miss any doses. If you miss a dose of TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET, take it as soon as you remember that day. Do not take more than 1 dose of TENOFOVIR DISOPROXIL FUMARATE, LAMIVUDINE & EFAVIRENZ TABLET in a day. Do not take 2 doses at the same time. Call your doctor or pharmacist if you are not sure what to do.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

The most common side effects are:

Nervous system symptoms such as dizziness, trouble sleeping, drowsiness, trouble concentrating, unusual dreams

Headache Diarrhea Nausea Vomiting Rash Flatulence (intestinal gas) Tiredness

Itching

Allergic reaction (including swelling of the face, lips, tongue or throat)

Abdominal pain

High blood pressure

Hair loss

Sense of feeling ill.

You should report any new or continuing symptoms to your doctor right away. Your doctor may be able to help you manage these side effects.

SHELF LIFE: Refer label for shelf life.

PACKING:

-30 tablets pack in HDPE botTenofovir Disoproxil Fumarate, Lamivudine & Efavirenz , seal & label them

-Such 1 botTenofovir Disoproxil Fumarate, Lamivudine & Efavirenz is packed in an individual carton along with a package insert

MARKETED BY:

APRAZER

APRAZER Healthcare Pvt Ltd.

B-256 ,2nd. Floor, Naraina Phase -1,

New Delhi-110028, India

Web: www.aprazerhealthcare.com

TM-Trademark Under Registration