PRESCRIBING INFORMATION
Tenofovir Disoproxil Fumarate & Emtricitabine Tablets

TEMIRAZER®

GENERIC NAME:
Tenofovir Disoproxil Fumarate & Emtricitabine Tablets

COMPOSITION
Each film coated tablet contains:
Tenofovir Disoproxil Fumarate 300 mg
Emtricitabine 200mg
Colours : Titanium Dioxide & Indigo Carmine.

PHARMACOLOGY
Tenofovir Disoproxil Fumarate and Emtricitabine Tabletsis a fixed-dose combination of antiviral drugs emtricitabine and tenofovir disoproxil fumarate.
Tenofovir disoproxil fumarate is an acyclic nucleoside phosphonate diester analogue 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 reverse transcriptase 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 alpha and beta, and mitochondrial DNA polymerase gamma.
Emtricitabine works by inhibiting reverse transcriptase, the enzyme that copies HIV RNA into new viral DNA. Emtricitabine is a synthetic nucleoside analogue of cytidine. It is phosphorylated by cellular enzymes to form emtricitabine 5'-triphosphate, which is responsible for the inhibition of HIV-1 reverse transcriptase. It competes with the natural substrate deoxycytidine 5'-triphosphate and incorporates into nascent viral DNA, resulting in early chain termination. Therefore emtricitabine inhibits the activity of HIV-1 reverse transcriptase (RT) both by competing with the natural substrate deoxycytidine 5'-triphosphate and by its incorporation into viral DNA. By inhibiting HIV-1 reverse transcriptase, emtricitabine can help to lower the amount of HIV, or "viral load", in a patient's body and can indirectly increase the number of immune system cells (called T cells or CD4+ T-cells). Both of these changes are associated with healthier immune systems and decreased likelihood of serious illness.

PHARMACOKINETICS
Emtricitabine: Following oral administration of emtricitabine tablets, emtricitabine is rapidly absorbed with peak plasma concentrations occurring at 1–2 hours post-dose. Less than 4% of emtricitabine binds to human plasma proteins in vitro and the binding is independent of concentration over the range of 0.02–200 µg/mL. Following administration of radiolabelled emtricitabine, approximately 86% is recovered in the urine and 13% is recovered as metabolites. The metabolites of emtricitabine include 3′-sulfoxide diastereomers and their glucuronic acid conjugate. Emtricitabine is eliminated by a combination of glomerular filtration and active tubular secretion. Following a single oral dose of emtricitabine, the plasma emtricitabine half-life is approximately 10 hours.
Tenofovir Disoproxil Fumarate: The pharmacokinetic properties of tenofovir disoproxil fumarate are summarized in Table 6. Following oral administration of Tenofovir Disoproxil Fumarate:, maximum tenofovir serum concentrations are achieved in 1.0 ± 0.4 hour. Less than 0.7% of tenofovir binds to human plasma proteins in vitro and the binding is independent of concentration over the range of 0.01–25 µg/mL. Approximately 70–80% of the intravenous dose of tenofovir is recovered as unchanged drug in the urine.
Tenofovir is eliminated by a combination of glomerular filtration and active tubular secretion. Following a single oral dose of Tenofovir Disoproxil Fumarate:, the terminal elimination half-life of tenofovir is approximately 17 hours.

INDICATIONS
Tenofovir Disoproxil Fumarate & Emtricitabine Tablets is a combination of Tenofovir Disoproxil Fumarate & Emtricitabine, both nucleoside analogue HIV-1 reverse transcriptase inhibitors.
Tenofovir Disoproxil Fumarate & Emtricitabine Tablets is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients 12 years of age and older.
Tenofovir Disoproxil Fumarate & Emtricitabine Tablets 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.

DOSAGE AND ADMINISTRATION:
Treatment of HIV-1 Infection
• Recommended dose in adults and pediatric patients (12 years of age and older and weighing greater than or equal to 35 kg): One tablet once daily taken orally with or without food.
• Recommended dose in renally impaired HIV-1 infected adult patients: Creatinine clearance 30-49 mL/min: 1 tablet every 48 hours. CrCl below 30 mL/min or hemodialysis:
Pre-exposure Prophylaxis
• Recommended dose in HIV-1 uninfected adults: One tablet once daily taken orally with or without food.
• Recommended dose in renally impaired HIV-uninfected individuals: Do not useTenofovir Disoproxil Fumarate and Emtricitabine Tablets in HIV-uninfected individuals if CrCl is below 60 mL/min. If a decrease in CrCl is observed in uninfected individuals while usingTenofovir Disoproxil Fumarate and Emtricitabine Tabletsfor PrEP, evaluate potential causes and re-assess potential risks and benefits of continued use.

CONTRAINDICATIONS:
Do not useTenofovir Disoproxil Fumarate and Emtricitabine Tabletsfor pre-exposure prophylaxis in individuals with unknown or positive HIV-1 status.Tenofovir Disoproxil Fumarate and Emtricitabine Tabletsshould be used in HIV-infected patients only in combination with other antiretroviral agents.

PRECAUTIONS AND WARNING:
• Recommended dose in renally impaired HIV-uninfected individuals: Do not useTenofovir Disoproxil Fumarate and Emtricitabine Tablets in HIV-uninfected individuals if CrCl is below 60 mL/min. If a decrease in CrCl is observed in uninfected individuals while usingTenofovir Disoproxil Fumarate and Emtricitabine Tabletsfor PrEP, evaluate potential causes and re-assess potential risks and benefits of continued use.
• New onset or worsening renal impairment: Can include acute renal failure and Fanconi syndrome. Assess creatinine clearance (CrCl) before initiating treatment with Tenofovir Disoproxil Fumarate & Emtricitabine Tablets Monitor CrCl and serum phosphorus in patients at risk. Avoid administering Tenofovir Disoproxil Fumarate and Emtricitabine Tabletswith concurrent or recent use of nephrotoxic drugs.
• Coadministration with Other Products: Do not use with drugs containing emtricitabine or tenofovir disoproxil fumarate including efavirenz + emtricitabine + tenofovir disoproxil fumarate, emtricitabine+rilpivirine+tenofovir, emtricitabine, tenofovir Disoproxil Fumarate; or with drugs containing lamivudine. Do not administer in combination with adefovir dipivoxil,.

SIDE EFFECTS:
In HIV1 infected patients, the most common adverse reactions (incidence greater than or equal to 10%) are diarrhea, nausea, fatigue, headache, dizziness, depression, insomnia, abnormal dreams, and rash.
In HIV-1 uninfected individuals in PrEP trials, adverse reactions that were reported by more than 2% of -Tenofovir Disoproxil Fumarate and Emtricitabine Tabletssubjects and more frequently than by placebo subjects were headache, abdominal pain and weight decreased.

DRUG INTERACTIONS
Didanosine: Tenofovir disoproxil fumarate increases didanosine concentrations. Use with caution and monitor for evidence of didanosine toxicity (e.g., pancreatitis, neuropathy) when coadministered. Consider dose reductions or discontinuations of didanosine if warranted.
• Atazanavir: Coadministration decreases atazanavir concentrations and increases tenofovir concentrations. Use atazanavir withTenofovir Disoproxil Fumarate and Emtricitabine Tabletsonly with ritonavir; monitor for evidence of tenofovir toxicity.

OVERDOSAGE
If overdose occurs, the patient must be monitored for evidence of toxicity, and standard supportive treatment applied as necessary.
Emtricitabine: Limited clinical experience is available at doses higher than the therapeutic dose of Emtricitabine. In one clinical pharmacology trial, single doses of emtricitabine 1200 mg were administered to 11 subjects. No severe adverse reactions were reported.
Hemodialysis treatment removes approximately 30% of the emtricitabine dose over a 3-hour dialysis period starting within 1.5 hours of emtricitabine dosing (blood flow rate of 400 mL/min and a dialysate flow rate of 600 mL/min). It is not known whether emtricitabine can be removed by peritoneal dialysis.
Tenofovir Disoproxil Fumarate: Limited clinical experience at doses higher than the therapeutic dose of Tenofovir Disoproxil Fumarate 300 mg is available. In one trial, 600 mg tenofovir disoproxil fumarate was administered to 8 subjects orally for 28 days, and no severe adverse reactions were reported. The effects of higher doses are not known.
Tenofovir is efficiently removed by hemodialysis with an extraction coefficient of approximately 54%. Following a single 300 mg dose of Tenofovir Disoproxil Fumarate, a four-hour hemodialysis session removed approximately 10% of the administered tenofovir dose.

PACKING: HDPE Bottle pack of 30 /60 tablets and packed in a unit carton along with package insert.
SHELF LIFE: Refer Label for the Shelf Life

STORAGE INSTRUCTIONS:
Store below 30ºC. Protect from light.

Keep this medicine out of the sight and reach of children.

Do not store above 30°C. Store in the original container.

Do not use this medicine after the expiry date which is stated on the bottle.
The expiry date refers to the last day of that month.
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

MARKETED BY:

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