To be sold by retail on the prescription of "Gastroenterologist/Hepatologist only"

PRESCRIBING INFORMATION

TAFGEN -25

TENOFOVIR ALAFENAMIDE TABLETS IP 25 mg

For India Only

WARNING:

POST TREATMENT SEVERE ACUTE EXACERBATION OF HEPATITIS B

Discontinuation of anti-hepatitis B therapy may result in severe acute exacerbations of hepatitis B. Hepatic function should be monitored closely in patients who discontinue Tenofovir alafenamide. If appropriate, resumption of anti-hepatitis B therapy may be warranted.

1. Generic Name

Tenofovir Alafenamide Tablets IP 25mg

2. Qualitative and Quantitative Composition

Each film coated tablet contains:

Tenofovir Alafenamide Fumarate IP

Eq. to Tenofovir Alafenamide…….. 25 mg

Excipients……..q.s.

Colours: Ferric oxide USP-NF Red, Ferrosoferric Oxide USP-NF and Titanium Dioxide IP.

3. Dosage Form & Strength

25 mg film coated tablets for oral use

4. Clinical Particulars

4.1 Therapeutic Indications

It is indicated for the treatment of chronic Hepatitis B virus infection in adults with compensated liver disease.

4.2 Posology and method of administration

Testing Prior to Initiation of Tenofovir alafenamide

Prior to initiation of Tenofovir alafenamide, patients should be tested for HIV-1 infection. Tenofovir alafenamide alone should not be used in patients with HIV-1 infection.

Prior to or when initiating Tenofovir alafenamide, and during treatment with Tenofovir alafenamide on a clinically appropriate schedule, assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein in all patients. In patients with chronic kidney disease, also assess serum phosphorus.

Therapy should be initiated by a physician experienced in the management of chronic hepatitis B.

Adults : The recommended dosage of Tenofovir alafenamide is one tablet taken orally once daily with food.

Pediatrics (< 18 years of age) : Safety and effectiveness of Tenofovir alafenamide in pediatric patients less than 18 years of age have not been established.

Geriatrics (≥ 65 years of age) : No dose adjustment is required in patients over the age of 65 years.

Hepatic Impairment : No dose adjustment of Tenofovir alafenamide is required in patients with mild hepatic impairment.

Tenofovir alafenamide is not recommended in patients with decompensated (Child-Pugh B or C) hepatic impairment.

Renal Impairment : No dosage adjustment of Tenofovir alafenamide is required in patients with estimated creatinine clearance ≥15 mL per minute, or in patients with end stage renal disease (ESRD; estimated creatinine clearance below 15 mL per minute) who are receiving chronic hemodialysis. On days of hemodialysis, administer Tenofovir alafenamide after completion of hemodialysis treatment.

Tenofovir alafenamide is not recommended in patients with ESRD who are not receiving chronic hemodialysis.

Method of administration

Oral administration. Tenofovir Alafenamide film-coated tablets should be taken with food.

4.3 Contraindications

It is contraindicated in patients with known hypersensitivity to Tenofovir alafenamide or to any other component of the formulation.

4.4 Special warnings and precautions for use

HBV transmission

Patients must be advised that Tenofovir alafenamide does not prevent the risk of transmission of HBV to others through sexual contact or contamination with blood. Appropriate precautions must continue to be used.

Patients with decompensated liver disease

There are limited data on the safety and efficacy of Tenofovir alafenamide in HBV-infected patients with decompensated liver disease and who have a Child Pugh Turcotte (CPT) score > 9 (i.e. class C). These patients may be at higher risk of experiencing serious hepatic or renal adverse reactions. Therefore, hepatobiliary and renal parameters should be closely monitored in this patient population.

Exacerbation of hepatitis

Flares on treatment : Spontaneous exacerbations in chronic hepatitis B are relatively common and are characterised by transient increases in serum alanine aminotransferase (ALT). After initiating antiviral therapy, serum ALT may increase in some patients. In patients with compensated liver disease, these increases in serum ALT are generally not accompanied by an increase in serum bilirubin concentrations or hepatic decompensation. Patients with cirrhosis may be at a higher risk for hepatic decompensation following hepatitis exacerbation, and therefore should be monitored closely during therapy.

Flares after treatment discontinuation : Acute exacerbation of hepatitis has been reported in patients who have discontinued treatment for hepatitis B, usually in association with rising HBV DNA levels in plasma. The majority of cases are self-limited but severe exacerbations, including fatal outcomes, may occur after discontinuation of treatment for hepatitis B. Hepatic function should be monitored at repeated intervals with both clinical and laboratory follow-up for at least 6 months after discontinuation of treatment for hepatitis B. If appropriate, resumption of hepatitis B therapy may be warranted. In patients with advanced liver disease or cirrhosis, treatment discontinuation is not recommended since post-treatment exacerbation of hepatitis may lead to hepatic decompensation. Liver flares are especially serious, and sometimes fatal in patients with decompensated liver disease.

Renal impairment

Patients with creatinine clearance < 30 mL/min

The use of Tenofovir alafenamide once daily in patients with CrCl ≥ 15 mL/min but < 30 mL/min and in patients with CrCl < 15 mL/min who are receiving haemodialysis is based on very limited pharmacokinetic data and on modelling and simulation. There are no safety data on the use of Tenofovir alafenamide to treat HBV-infected patients with CrCl < 30 mL/min.

The use of Tenofovir alafenamide is not recommended in patients with CrCl < 15 mL/min who are not receiving haemodialysis.

New Onset or Worsening Renal Impairment

Renal impairment, including cases of acute renal failure and Fanconi syndrome (renal tubular injury with severe hypophosphatemia), has been reported with the use of tenofovir prodrugs in both animal toxicology studies and human trials. In clinical trials of Tenofovir alafenamide, there have been no cases of Fanconi syndrome or Proximal Renal Tubulopathy (PRT).

Patients taking tenofovir prodrugs who have impaired renal function and those taking nephrotoxic agents, including non-steroidal anti-inflammatory drugs, are at increased risk of developing renal-related adverse reactions.

Prior to or when initiating Tenofovir alafenamide, and during treatment with Tenofovir alafenamide on a clinically appropriate schedule, assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein in all patients. In patients with chronic kidney disease, also assess serum phosphorus. Discontinue Tenofovir alafenamide in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome.

Nephrotoxicity

A potential risk of nephrotoxicity resulting from chronic exposure to low levels of tenofovir due to dosing with tenofovir alafenamide cannot be excluded.

Patients co-infected with HBV and hepatitis C or D virus

There are no data on the safety and efficacy of Tenofovir alafenamide in patients co-infected with hepatitis C or D virus. Co-administration guidance for the treatment of hepatitis C should be followed.

Hepatitis B and HIV co-infection

HIV antibody testing should be offered to all HBV-infected patients whose HIV-1 infection status is unknown before initiating therapy with Tenofovir alafenamide. In patients who are co-infected with HBV and HIV, Tenofovir alafenamide should be co-administered with other antiretroviral agents to ensure that the patient receives an appropriate regimen for treatment of HIV.

Co-administration with other medicinal products

Tenofovir alafenamide should not be co-administered with products containing tenofovir alafenamide, tenofovir disoproxil fumarate or adefovir dipivoxil.

Co-administration of Tenofovir alafenamide with certain anticonvulsants (e.g. carbamazepine, oxcarbazepine, phenobarbital and phenytoin), antimycobacterials (e.g. rifampicin, rifabutin and rifapentine) or St. John's wort, all of which are inducers of P-glycoprotein (P-gp) and may decrease tenofovir alafenamide plasma concentrations, is not recommended.

Co-administration of Tenofovir alafenamide with strong inhibitors of P-gp (e.g. itraconazole and ketoconazole) may increase tenofovir alafenamide plasma concentrations. Co-administration is not recommended.

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, another prodrug of tenofovir, alone or in combination with other antiretrovirals. Treatment with Tenofovir alafenamide 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).

4.5 Drug Interactions

Potential for other drugs to affect tenofovir alafenamide : Tenofovir alafenamide is a substrate of P-glycoprotein (P-gp) and BCRP. Drugs that strongly affect P-gp and BCRP activity may lead to changes in tenofovir alafenamide absorption. Drugs that induce P-gp activity are expected to decrease the absorption of tenofovir alafenamide, resulting in decreased plasma concentrations of tenofovir alafenamide, which may lead to loss of therapeutic effect of Tenofovir alafenamide. Co-administration of Tenofovir alafenamide with other drugs that inhibit P-gp and BCRP may increase the absorption and plasma concentration of tenofovir alafenamide.

Drugs affecting renal function: Because tenofovir is primarily excreted by the kidneys by a combination of glomerular filtration and active tubular secretion, co-administration of Tenofovir alafenamide with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of tenofovir and other renally eliminated drugs and this may increase the risk of adverse reactions. Some examples of drugs that are eliminated by active tubular secretion include, but are not limited to, acyclovir, cidofovir, ganciclovir, valacyclovir, valganciclovir, aminoglycosides (e.g., gentamicin), and high-dose or multiple NSAIDs.

Established and other potentially significant interactions

The below table provides a listing of established or potentially clinically significant drug interactions.

Established and other potentially significant drug interactions [a]

Concomitant Drug Class: Drug Name	Effect on Concentrationb	Clinical Comment
Anticonvulsants: Carbamazepine[c]* Oxcarbazepine* Phenobarbital* phenytoin*	↓ tenofovir alafenamide	When co-administered with carbamazepine, the tenofovir alafenamide dose should be increased to two tablets once daily. Co-administration of Tenofovir alafenamide with oxcarbazepine, phenobarbital, or phenytoin is not recommended.
Antimycobacterial: Rifabutin * Rifampin* Rifapentine*	↓ tenofovir alafenamide	Co-administration of Tenofovir alafenamide with rifabutin, rifampin or rifapentine is not recommended.
Herbal Products: St. John's wort* (Hypericum perforatum)	↓ tenofovir alafenamide	Co-administration of Tenofovir alafenamide with St. John's wort is not recommended.

[a] This table is not all inclusive; [b] ↓ = decrease; [c] Indicates that a drug interaction study was conducted; * P-gp inducer

Drugs without clinically significant interactions with tenofovir alafenamide

Based on drug interaction studies conducted with Tenofovir alafenamide, no clinically significant drug interactions have been observed with: ethinyl estradiol, itraconazole, ketoconazole, ledipasvir/sofosbuvir, Sofosbuvir/velpatasvir/voxilaprevir, midazolam, norgestimate, sertraline, and sofosbuvir.

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy : There are no human data on the use of Tenofovir alafenamide in pregnant women to inform a drug associated risks of adverse fetal developmental outcome. In animal studies, no adverse developmental effects were observed when tenofovir alafenamide was administered during the period of organogenesis at exposure equal to or 51 times (rats and rabbits, respectively) the tenofovir alafenamide exposure at the recommended daily dose of tenofovir alafenamide. No adverse effects were observed in the offspring when tenofovir disoproxil fumarate was administered through lactation at tenofovir exposures of approximately 12 times the exposure at the recommended daily dosage of Tenofovir alafenamide.

The background risk of major birth defects and miscarriage for the indicated population is unknown. The use of Tenofovir alafenamide may be considered during pregnancy, if necessary.

Lactation : It is not known whether tenofovir alafenamide is secreted in human milk. However, in animal studies it has been shown that tenofovir is secreted into milk. There is insufficient information on the effects of tenofovir in newborns/infants.

A risk to the breastfed child cannot be excluded; therefore, tenofovir alafenamide should not be used during breast-feeding.

Pediatric Use : Safety and effectiveness of Tenofovir alafenamide in pediatric patients less than 18 years of age have not been established.

Geriatric Use : Clinical trials of Tenofovir alafenamide did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

Renal Impairment : No dosage adjustment of Tenofovir alafenamide is required in patients with mild, moderate, or severe renal impairment. Tenofovir alafenamide is not recommended in patients with end stage renal disease (estimated creatinine clearance below 15 mL per minute).

Hepatic Impairment : No dosage adjustment of Tenofovir alafenamide is required in patients with mild hepatic impairment (Child-Pugh A). The safety and efficacy of Tenofovir alafenamide in patients with decompensated cirrhosis (Child-Pugh B or C) have not been established; therefore Tenofovir alafenamide is not recommended in patients with decompensated (Child-Pugh B or C) hepatic impairment.

4.7 Effects on ability to drive and use machines.

Tenofovir alafenamide has no or negligible influence on the ability to drive and use machines. Patients should be informed that dizziness has been reported during treatment with Tenofovir alafenamide.

4.8 Undesirable Effects.

Gastrointestinal disorders:
Common: Diarrhoea, vomiting, nausea, abdominal pain, abdominal distension, flatulence.

General disorders and administration site conditions
Common: Fatigue

Nervous system disorders
Very Common: Headache
Common: Dizziness

Skin and subcutaneous tissue disorders
Common: Rash, pruritus, angioedema and urticaria is Uncommon AEs which are identified through post-marketing surveillance.

Hepatobiliary disorders
Common: Increased ALT

Musculoskeletal and connective tissue disorders
Common: Arthralgia

Reporting of suspected adverse reactions

Health care professionals, patients/consumers are advised to closely monitor the possibility of the above ADRs associated with the use of the above drugs. If such reactions are encountered, please report to the Hetero either by filling of Suspect Adverse Drug Reactions Reporting Form **(form.heteroworld.com)** or by **Hetero Helpline No.1800-120-8689** and for all India safety cases and complaints, please write to drugsafetyindia@heterodrugs.com.

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4.9 Overdose

If overdose occurs the patient must be monitored for evidence of toxicity. Treatment of overdose with Tenofovir alafenamide consists of general supportive measures including monitoring of vital signs as well as observation of the clinical status of the patient. Tenofovir is efficiently removed by haemodialysis with an extraction coefficient of approximately 54%.

5. Pharmacological Properties

5.1 Mechanism of action

Tenofovir alafenamide is a phosphonamidate prodrug of tenofovir (2'-deoxyadenosine monophosphate analog). Tenofovir alafenamide as a lipophilic cell-permeant compound enters primary hepatocytes by passive diffusion and by the hepatic uptake transporters OATP1B1 and OATP1B3. Tenofovir alafenamide is then converted to tenofovir through hydrolysis primarily by carboxylesterase 1 (CES1) in primary hepatocytes. Intracellular tenofovir is subsequently phosphorylated by cellular kinases to the pharmacologically active metabolite tenofovir diphosphate. Tenofovir diphosphate inhibits HBV replication through incorporation into viral DNA by the HBV reverse transcriptase, which results in DNA chain-termination.

Tenofovir diphosphate is a weak inhibitor of mammalian DNA polymerases that include mitochondrial DNA polymerase γ and there is no evidence of toxicity to mitochondria in cell culture.

5.2 Pharmacodynamic properties

Antiviral Activity in Cell Culture : The antiviral activity of tenofovir alafenamide was assessed in a transient transfection assay using HepG2 cells against a panel of HBV clinical isolates representing genotypes A-H. The EC50 (50% effective concentration) values for tenofovir alafenamide ranged from 34.7 to 134.4 nM, with an overall mean EC_{50} value of 86.6 nM. The CC_{50} (50% cytotoxicity concentration) values in HepG2 cells were greater than 44,400 nM. In cell culture combination antiviral activity studies of tenofovir with the HBV nucleoside reverse transcriptase inhibitors entecavir, lamivudine, and telbivudine, no antagonistic activity was observed.

Cardiac Electrophysiology : In a thorough QT/QTc study in 48 healthy subjects, tenofovir alafenamide at the recommended dose or at a dose 5 times the recommended dose did not affect the QT/QTc interval and did not prolong the PR interval.

Resistance : In a pooled analysis of patients receiving tenofovir alafenamide, sequence analysis was performed on paired baseline and on-treatment HBV isolates for patients who either experienced virologic breakthrough (2 consecutive visits with HBV DNA ≥ 69 IU/mL after having been < 69 IU/mL, or 1.0 log_{10} or greater increase in HBV DNA from nadir) or patients with HBV DNA ≥ 69 IU/mL at Week 96 or at early discontinuation at or after Week 24. In analyses at Week 48 (N = 20) and Week 96 (N = 72), no amino acid substitutions associated with resistance to tenofovir alafenamide were identified in these isolates (genotypic and phenotypic analyses).

Cross-resistance : The antiviral activity of tenofovir alafenamide was evaluated against a panel of isolates containing nucleos(t)ide reverse transcriptase inhibitor mutations in HepG2 cells. HBV isolates expressing the rtV173L, rtL180M, and rtM204V/I substitutions associated with resistance to lamivudine remained susceptible to tenofovir alafenamide (< 2-fold change in EC_{50}). HBV isolates expressing the rtL180M, rtM204V plus rtT184G, rtS202G, or rtM250V substitutions associated with resistance to entecavir remained susceptible to tenofovir alafenamide. HBV isolates expressing the rtA181T, rtA181V, or rtN236T single substitutions associated with resistance to adefovir remained susceptible to tenofovir alafenamide; however, the HBV isolate expressing rtA181V plus rtN236T exhibited reduced susceptibility to tenofovir alafenamide (3.7-fold change in EC_{50}). The clinical relevance of these substitutions is not known.

5.3 Pharmacokinetic properties

Absorption : Following oral administration of tenofovir alafenamide under fasted conditions in adult patients with chronic hepatitis B, peak plasma concentrations of tenofovir alafenamide were observed approximately 0.48 hours post-dose. Based on Phase 3 population pharmacokinetic analysis in subjects with CHB, mean steady state $AUC_{0\text{-}24}$ for tenofovir alafenamide (N = 698) and tenofovir (N = 856) were 0.22 μghr/mL and 0.32 μghr/mL, respectively. Steady state C_{max} for tenofovir alafenamide and tenofovir were 0.18 and 0.02 μg/mL, respectively. Relative to fasting conditions, the administration of a single dose of tenofovir alafenamide with a high fat meal resulted in a 65% increase in tenofovir alafenamide exposure.

Distribution : The binding of tenofovir alafenamide to human plasma proteins in samples collected during clinical trials was approximately 80%. The binding of tenofovir to human plasma proteins is less than 0.7% and is independent of concentration over the range of 0.01–25 μg/mL.

Metabolism : Metabolism is a major elimination pathway for tenofovir alafenamide in humans, accounting for > 80% of an oral dose. *In vitro* studies have shown that tenofovir alafenamide is metabolized to tenofovir (major metabolite) by carboxylesterase-1 in hepatocytes; and by cathepsin A in PBMCs and macrophages. *In vivo*, tenofovir alafenamide is hydrolysed within cells to form tenofovir (major metabolite), which is phosphorylated to the active metabolite, tenofovir diphosphate.

In vitro, tenofovir alafenamide is not metabolized by CYP1A2, CYP2C8, CYP2C9, CYP2C19, or CYP2D6. Tenofovir alafenamide is minimally metabolized by CYP3A4.

Excretion : Renal excretion of intact tenofovir alafenamide is a minor pathway with < 1% of the dose eliminated in urine. Tenofovir alafenamide is mainly eliminated following metabolism to tenofovir. Tenofovir alafenamide and tenofovir have a median plasma half-life of 0.51 and 32.37 hours, respectively. Tenofovir is renally eliminated from the body by the kidneys by both glomerular filtration and active tubular secretion.

6. Nonclinical Properties

6.1 Animal Toxicology or Pharmacology

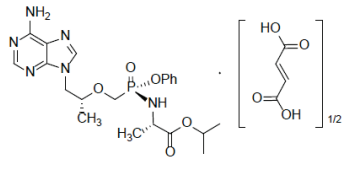
Non-clinical studies in rats and dogs revealed bone and kidney as the primary target organs of toxicity. Bone toxicity was observed as reduced BMD in rats and dogs at tenofovir exposures at least four times greater than those expected after administration of tenofovir alafenamide. A minimal infiltration of histiocytes was present in the eye in dogs at tenofovir alafenamide and tenofovir exposures of approximately 4 and 17 times greater, respectively, than those expected after administration of tenofovir alafenamide.

Tenofovir alafenamide was not mutagenic or clastogenic in conventional genotoxic assays.

Because there is a lower tenofovir exposure in rats and mice after tenofovir alafenamide administration compared to tenofovir disoproxil fumarate, carcinogenicity studies and a rat peri-postnatal study were conducted only with tenofovir disoproxil fumarate. No special hazard for humans was revealed in conventional studies of carcinogenic potential with tenofovir disoproxil (as fumarate) and toxicity to reproduction and development with tenofovir disoproxil (as fumarate) or tenofovir alafenamide. Reproductive toxicity studies in rats and rabbits showed no effects on mating, fertility, pregnancy or foetal parameters. However, tenofovir disoproxil fumarate reduced the viability index and weight of pups in a peri-postnatal toxicity study at maternally toxic doses. A long-term oral carcinogenicity study in mice showed a low incidence of duodenal tumours, considered likely related to high local concentrations in the gastrointestinal tract at the high dose of 600 mg/kg/day. The mechanism of tumour formation in mice and potential relevance for humans is uncertain.

7. Description

Tenofovir alafenamide, a hepatitis B virus (HBV) nucleoside analog reverse transcriptase inhibitor, is converted *in vivo* to tenofovir, an acyclic nucleoside phosphonate (nucleotide) analog of adenosine 5'-monophosphate. The chemical name of tenofovir alafenamide fumarate drug substance is L-alanine, N[(S)-[[(1R)-2-(6-amino-9H-purin-9-yl)-1-methylethoxy]methyl]phenoxyphosphinyl]-, 1 methylethyl ester, (2E)-2-butenedioate (2:1). It has an empirical formula of $C_{21}H_{29}O_5N_6P½(C_4H_4O_4)$ and a formula weight of 534.50 g/mol. It has the following structural formula:



Tenofovir alafenamide fumarate is a white to off-white or tan powder with a solubility of 4.7 mg per mL in water at 20 °C.

8. Pharmaceutical Particulars

8.1 Incompatibilities

Not Applicable

8.2 Shelf-life

See on Pack

8.3 Packing Information

Each HDPE Container: Contains 30 Tablets

8.4 Storage and handling instructions

Store protected from light and moisture, at a temperature not exceeding 30°C.

KEEP OUT OF REACH OF CHILDREN

Keep container tightly closed.

Dispense in original container.

Do not use if seal over bottle opening is broken or missing.

9. Patient Counselling Information

1) What is Tenofovir AF Tablets?

Tenofovir AF Tablets is a prescription medicine used to treat chronic Hepatitis B virus (HBV) infection in adults with compensated liver disease.

- Tenofovir AF Tablets may lower the amount of HBV in your body.
- Tenofovir AF Tablets may improve the condition of your liver.

It is not known if Tenofovir AF Tablets is safe and effective in children under 18 years of age.

2) What should I tell my healthcare provider before taking Tenofovir AF Tablets?

Before you take Tenofovir AF Tablets, tell your healthcare provider about all of your medical conditions, including if you:

- have HIV-1 infection. Your healthcare provider may test you for HIV-1 infection before you start Tenofovir AF Tablets. If you have both HBV and HIV-1, and you only take Tenofovir AF Tablets, the HIV-1 virus may develop resistance and become harder to treat.
- have end stage renal disease (ESRD).
- are pregnant or plan to become pregnant. It is not known if Tenofovir AF Tablets will harm your unborn baby. Tell your healthcare provider if you become pregnant during treatment with Tenofovir AF Tablets.
- are breastfeeding or plan to breastfeed. It is not known if Tenofovir AF Tablets passes into your breast milk. Talk with your healthcare provider about the best way to feed your baby.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Some medicines may affect how Tenofovir AF Tablets works.

- Keep a list of your medicines and show it to your healthcare provider and pharmacist when you get a new medicine. You can ask your healthcare provider or pharmacist for a list of medicines that interact with Tenofovir AF Tablets.
- Do not start a new medicine without telling your healthcare provider. Your healthcare provider can tell you if it is safe to take Tenofovir AF Tablets with other medicines.

3) How should I take Tenofovir AF Tablets?

- Take Tenofovir AF Tablets exactly as your healthcare provider tells you to take it.
- Take Tenofovir AF Tablets 1 time each day.
- Take Tenofovir AF Tablets with food.
- If you are on dialysis, on your dialysis days, take your daily dose of Tenofovir AF Tablets following dialysis.
- Do not change your dose or stop taking Tenofovir AF Tablets without first talking with your healthcare provider. Stay under a healthcare provider's care when taking Tenofovir AF Tablets.
- Do not miss a dose of Tenofovir AF Tablets.
- If you take too much Tenofovir AF Tablets, call your healthcare provider or go to the nearest hospital emergency room right away.
- When your Tenofovir AF Tablets supply starts to run low, get more from your healthcare provider or pharmacy. This is very important because your HBV infection may get worse (flare-up) if you stop taking Tenofovir AF Tablets.

4) What is the most important information I should know about Tenofovir AF Tablets?

Tenofovir AF Tablets can cause serious side effects, including:

- Worsening of hepatitis B infection. Your hepatitis B (HBV) infection may become worse (flare-up) if you take Tenofovir AF Tablets and then stop taking it. A "flare-up" is when your HBV infection suddenly returns in a worse way than before.
- Do not run out of Tenofovir AF Tablets. Refill your prescription or talk to your healthcare provider before your Tenofovir AF is all gone.
- Do not stop taking Tenofovir AF Tablets without first talking to your healthcare provider.
- If you stop taking Tenofovir AF Tablets, your healthcare provider will need to check your health often and do blood tests regularly for several months to check your HBV infection. Tell your healthcare provider about any new or unusual symptoms you may have after you stop taking Tenofovir AF Tablets.

5) What are the possible side effects of Tenofovir AF Tablets?

Tenofovir AF Tablets may cause serious side effects, including:

- See "What is the most important information I should know about Tenofovir AF Tablets?"
- New or worse kidney problems, including kidney failure. Your healthcare provider should do blood and urine tests to check your kidneys when starting and during treatment with Tenofovir AF Tablets. Your healthcare provider may tell you to stop taking Tenofovir AF Tablets if you develop new or worse kidney problems.
- Too much lactic acid in your blood (lactic acidosis). Too much lactic acid is a serious but rare medical emergency that can lead to death. Tell your healthcare provider right away if you get these symptoms: weakness or being more tired than usual, unusual muscle pain, being short of breath or fast breathing, stomach pain with nausea and vomiting, cold or blue hands and feet, feel dizzy or lightheaded, or a fast or abnormal heartbeat.
- Severe liver problems. In rare cases, severe liver problems can happen that can lead to death. Tell your healthcare provider right away if you get these symptoms: skin or the white part of your eyes turns yellow, dark "tea-colored" urine, light-colored stools, loss of appetite for several days or longer, nausea, or stomach-area pain.

The most common side effect of tenofovir alafenamide is headache. Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of Tenofovir AF Tablets. For more information, ask your healthcare provider or pharmacist.

Health care professionals, patients/consumers are advised to closely monitor the possibility of the above ADRs associated with the use of the above drugs. If such reactions are encountered, please report to the Hetero either by filling of Suspect Adverse Drug Reactions Reporting Form (form.heteroworld.com) or by Hetero Helpline No.1800-120-8689 and for all India safety cases and complaints, please write to drugsafetyindia@heterodrugs.com.

By reporting side effects, you can help provide more information on the safety of this product

6) How should I store Tenofovir AF Tablets?

- Store protected from light and moisture, at a temperature not exceeding 30°C.
- KEEP OUT OF REACH OF CHILDREN
- Keep container tightly closed.
- Dispense in original container.
- Do not use if seal over bottle opening is broken or missing.

General information about the safe and effective use of Tenofovir AF Tablets.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use Tenofovir AF Tablets for a condition for which it was not prescribed. Do not give Tenofovir AF Tablets to other people, even if they have the same symptoms you have. It may harm them. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about Tenofovir AF Tablets that is written for health professionals.

Tafgen -25 is manufactured under a license from Gilead Sciences, Inc.

For use in India Only, Not for Export.

10. Details of Manufacturer

Hetero Labs Limited (Unit-II)

Village: Kalyanpur, Chakkan Road, Tehsil: Baddi, Distt.: Solan, Himachal Pradesh - 173205.

11. Details of Marketed

Marketed by:
Genygi Life Sciences Private Limited
SS - 29, Second Floor, Aditya Mega Mall,
Plot # 9D, Delhi - 110032

12. Details of permission or licence number with date

MF-ND-40/2018 dated 05th Mar 2018

13. Date of revision

31-08-2024

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