TENVIR AF Tablets (Tenofovir alafenamide)

**Black Box Warning**

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 with both clinical and laboratory follow-up for at least several months in patients who discontinue TENVIR AF. If appropriate, resumption of anti-hepatitis B therapy may be warranted.

**Composition**

TENVIR AF Tablets
Each film coated tablet contains:
Tenofovir alafenamide hemifumarate
Eq.to Tenofovir alafenamide.............. 25 mg
Excipients.....................................q.s.
Colours: Ferric oxide USP-NF Red,
Black iron oxide & Titanium dioxide IP.

**Dosage Form**

Tablet for oral use

**Pharmacology**

► Pharmacodynamics

*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.

*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 EC50 value of 86.6 nM. The CC50 (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. Tenofovir alafenamide is an antiviral drug against the hepatitis B virus (HBV).

Pharmacokinetics
Absorption and Bioavailability
Following oral administration of tenofovir alafenamide under fasted conditions in adult patients with chronic hepatitis B, peak plasma concentrations were observed approximately 0.48 hours post dose. The steady-state mean $C_{\text{max}}$ and $AUC_{\text{last}}$ for tenofovir alafenamide were $0.25 \pm 0.11 \mu g/mL$ and $0.15 \pm 0.06 \mu g\cdot hr/ml$, respectively.

Effect of Food on Oral Absorption
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. This difference in exposure is not considered clinically relevant and tenofovir alafenamide may be administered without regard to food.

Distribution
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 micrograms per mL. The binding of tenofovir alafenamide to human plasma proteins in samples collected during clinical trials was approximately 80%.

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 peripheral blood mononuclear cells (PBMCs) and macrophages. In vivo, tenofovir alafenamide is hydrolyzed within cells to form tenofovir (major metabolite), which is phosphorylated to the active metabolite, tenofovir diphosphate. In clinical studies in patients with chronic hepatitis B, a 25 mg oral dose of tenofovir alafenamide resulted in tenofovir diphosphate concentrations 7.6-fold higher in PBMCs and 89% lower concentrations of tenofovir in plasma as compared to a 300 mg oral dose of tenofovir disoproxil fumarate in tenofovir disoproxil fumarate.

In vitro, tenofovir alafenamide is not metabolized by CYP1A2, CYP2C8, CYP2C9, CYP2C19, or CYP2D6. Tenofovir alafenamide is minimally metabolized by CYP3A4. Upon co-administration with the strong CYP3A inducer probe carbamazepine, tenofovir alafenamide exposure was not affected to a clinically meaningful extent. Tenofovir alafenamide is not an inhibitor of CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, or UGT1A1. Tenofovir alafenamide is not an inhibitor or inducer of CYP3A in vivo.

Excretion
Tenofovir alafenamide is 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 by both glomerular filtration and active tubular secretion. Unlike tenofovir, tenofovir alafenamide is not a substrate for renal transporters OAT1 and OAT3. Renal excretion of intact tenofovir alafenamide is a minor pathway with less than 1% of the dose eliminated in urine. The pharmacologically active metabolite, tenofovir diphosphate, has a half-life of 150-180 hours within PBMCs.

Special Populations
Gender
No clinically relevant differences in tenofovir alafenamide or tenofovir pharmacokinetics due to gender have been identified.

Race/Ethnicity
No clinically relevant differences in tenofovir alafenamide or tenofovir pharmacokinetics due to race have been identified.

Geriatric
Limited data in subjects aged 65 years and over suggest a lack of clinically relevant differences in tenofovir alafenamide or tenofovir pharmacokinetics.

Renal Impairment
Relative to subjects with normal renal function (estimated creatinine clearance ≥90 mL/min), the tenofovir alafenamide and tenofovir systemic exposures in subjects with severe renal impairment were 1.9-fold and 5.7-fold higher, respectively. The pharmacokinetics of tenofovir alafenamide have not been evaluated in patients with creatinine clearance <15 mL per minute.

Hepatic Impairment
Relative to subjects with normal hepatic function, tenofovir alafenamide and tenofovir systemic exposures were 7.5% and 11% lower in subjects with mild hepatic impairment, respectively.

HIV and/or Hepatitis C Virus Co-infection
The pharmacokinetics of tenofovir alafenamide have not been fully evaluated in subjects coinfected with HIV and/or hepatitis C virus.

Indications
TENVIR AF Tablets are indicated for the treatment of chronic HBV infection in adults with compensated liver disease.

Dosage And Administration

Testing Prior to the Initiation of Therapy
Prior to initiation of TENVIR AF, patients should be tested for HIV-1 infection. TENVIR AF alone should not be used in patients with HIV infection.

It is recommended that serum creatinine, serum phosphorous, estimated creatinine clearance, urine glucose, and urine protein be assessed before initiating TENVIR AF and during therapy in all patients as clinically appropriate.

Recommended Dosage in Adults
The recommended dosage of TENVIR AF is 25 mg (one tablet) taken orally once daily with food.

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

Dosage in Patients with 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 <15 mL per minute).

Dosage in Patients with Hepatic Impairment
No dosage adjustment of tenofovir alafenamide is required in patients with mild hepatic impairment (Child-Pugh A). Tenofovir alafenamide is not recommended in patients with decompensated (Child-Pugh B or C) hepatic impairment.

**Contraindications**

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

**Warnings And Precautions**

- **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 disoproxil fumarate 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).

- **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.

- **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 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.
Due to the risk of development of HIV-1 resistance, tenofovir alafenamide alone is not recommended for the treatment of HIV-1 infection. The safety and efficacy of tenofovir alafenamide have not been established in patients co-infected with HBV and HIV-1. HIV antibody testing should be offered to all HBV-infected patients before initiating therapy with tenofovir alafenamide, and, if positive, an appropriate antiretroviral combination regimen that is recommended for patients co-infected with HIV-1 should be used.

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. It is recommended that serum creatinine, serum phosphorous, estimated creatinine clearance, urine glucose, and urine protein be assessed before initiating tenofovir alafenamide and during therapy in all patients as clinically appropriate. Discontinue tenofovir alafenamide in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome.

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

There are no 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.

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 (see Table 1). 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.

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.

Table 1 provides a listing of established or potentially clinically significant drug interactions. The drug
interactions described are based on studies conducted with tenofovir alafenamide or are predicted drug interactions that may occur with tenofovir alafenamide. Information regarding potential drug–drug interactions with HIV antiretrovirals is not provided (see the prescribing information for emtricitabine/tenofovir alafenamide for interactions with HIV antiretrovirals). The table includes potentially significant interactions but is not all inclusive.

Table 1: Established and Other Potentially Significant Drug Interactionsa

<table>
<thead>
<tr>
<th>Concomitant Drug Class: Drug Name</th>
<th>Effect on Concentrationb</th>
<th>Clinical Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticonvulsants: Carbamazepine* Oxcarbazepine* Phenobarbital* Phenytoin*</td>
<td>↓ tenofovir alafenamide</td>
<td>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.</td>
</tr>
<tr>
<td>Antimycobacterial: Rifabutin* Rifampin* Rifapentine*</td>
<td>↓ tenofovir alafenamide</td>
<td>Co-administration of tenofovir alafenamide with rifabutin, rifampin or rifapentine is not recommended.</td>
</tr>
<tr>
<td>Herbal Products: St. John’s wort* (Hypericum perforatum)</td>
<td>↓ tenofovir alafenamide</td>
<td>Co-administration of tenofovir alafenamide with St. John’s wort is not recommended.</td>
</tr>
</tbody>
</table>

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 the following: ethinyl estradiol, itraconazole, ketoconazole, ledipasvir/sofosbuvir, midazolam, norgestimate, sertraline, sofosbuvir, and sofosbuvir/velpatasvir.

Co-Administration with Other Medicinal Products

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

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.
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.

Pregnancy

Risk Summary

There are no human data on the use of tenofovir alafenamide in pregnant women to inform a drug-associated risk 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 (TDF) 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

Risk Summary

It is not known whether tenofovir alafenamide and its metabolites are present in human breast milk, affect human milk production, or have effects on the breastfed infant. Tenofovir has been shown to be present in the milk of lactating rats and rhesus monkeys after administration of TDF. 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 years and over to determine whether they respond differently from younger subjects.

Undesirable Effects

The following adverse reactions are discussed in other sections of the labelling:

- Lactic Acidosis/Severe Hepatomegaly with Steatosis
- Severe Acute Exacerbation of Hepatitis B
- New-Onset or Worsening of Renal Impairment

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice. Some of the common adverse events are as follows:

Gastrointestinal disorders: Diarrhoea, vomiting, nausea, abdominal pain, abdominal distension, flatulence.
General disorders and administration site conditions: Fatigue
Nervous system disorders: Headache, dizziness.
Skin and subcutaneous tissue disorders: Rash, pruritus
Hepatobiliary disorders: Increased ALT
Musculoskeletal and connective tissue disorders: Arthralgia

Adverse Reactions in Adult Subjects with Chronic Hepatitis B and Compensated Liver Disease

The safety assessment of tenofovir alafenamide was based on pooled data through the week 48 data analysis from 1,298 subjects in two randomized, double-blind, active-controlled trials, Study 108 and Study 110, in adult subjects with chronic hepatitis B and compensated liver disease. A total of 866 subjects received tenofovir alafenamide 25 mg once daily. The proportion of subjects who discontinued treatment with tenofovir alafenamide or tenofovir disoproxil fumarate due to adverse reactions of any severity was 1.0% and 1.2%, respectively. Table 2 displays the frequency of the adverse reaction (all grades) greater than or equal to 5% in the tenofovir alafenamide group.

Table 2: Adverse Reactionsa (All Grades) Reported in ≥5% of Subjects with Chronic HBV Infection and Compensated Liver Disease in Studies 108 and 110 (Week 48 Analysis)

<table>
<thead>
<tr>
<th></th>
<th>Tenofovir Alafenamide (N=866)</th>
<th>TDF (N=432)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>9%</td>
<td>8%</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>7%</td>
<td>6%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>6%</td>
<td>5%</td>
</tr>
<tr>
<td>Cough</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Nausea</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Back pain</td>
<td>5%</td>
<td>4%</td>
</tr>
</tbody>
</table>

a Frequencies of adverse reactions are based on all treatment-emergent adverse events, regardless of relationship to the study drug.

Renal Laboratory Tests

In a pooled analysis of Studies 108 and 110 in adult subjects with chronic hepatitis B and a median baseline eGFR of 106 and 105 mL per minute (for the tenofovir alafenamide and TDF groups, respectively), mean serum creatinine increased by less than 0.1 mg/dL and median serum phosphorus decreased by 0.1 mg/dL in both treatment groups. Median change from baseline in eGFR was -1.2 mL per minute in the tenofovir alafenamide group and -5.4 mL per minute in those receiving TDF. The long-term clinical significance of these renal laboratory changes on adverse reaction frequencies between tenofovir alafenamide and TDF is not known.

Decrease in Bone Mineral Density

In a pooled analysis of Studies 108 and 110, the mean percentage change in bone mineral density (BMD) from baseline to week 48 as assessed by dual-energy X-ray absorptiometry (DXA) was -0.6% with tenofovir alafenamide compared with -2.4% with TDF at the lumbar spine, and -0.2% compared with -1.9% at the total hip. BMD declines of 5% or greater at the lumbar spine were experienced by 6% of tenofovir alafenamide subjects and 20% of TDF subjects. BMD declines of 7% or greater at the femoral neck were
experienced by 3% of tenofovir alafenamide subjects and 6% of TDF subjects. The long-term clinical significance of these BMD changes is not known.

Laboratory Abnormalities

The frequency of laboratory abnormalities (grades 3–4) occurring in at least 2% of subjects receiving tenofovir alafenamide in Studies 108 and 110 are presented in Table 3.

Table 3: Laboratory Abnormalities (Grades 3–4) Reported in ≥2% of Subjects with Chronic HBV Infection and Compensated Liver Disease in Studies 108 and 110 (Week 48 analysis)

<table>
<thead>
<tr>
<th>Laboratory Parameter Abnormality</th>
<th>Tenofovir Alafenamide (N=866)</th>
<th>TDF (N=432)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT (&gt;5 × ULN)</td>
<td>8%</td>
<td>9%</td>
</tr>
<tr>
<td>Glycosuria (&gt;3+)</td>
<td>5%</td>
<td>1%</td>
</tr>
<tr>
<td>LDL-cholesterol (fasted) (&gt;190 mg/dL)</td>
<td>4%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>AST (&gt;5 × ULN)</td>
<td>3%</td>
<td>5%</td>
</tr>
<tr>
<td>Creatine kinase (≥10 × ULN)</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Serum amylase (&gt;2.0 × ULN)</td>
<td>3%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Frequencies are based on treatment-emergent laboratory abnormalities.

Amylase and Lipase Elevations and Pancreatitis

In Studies 108 and 110, 7 subjects treated with tenofovir alafenamide with elevated amylase levels had associated symptoms, such as nausea, low back pain, abdominal tenderness, biliary pancreatitis and pancreatitis. Of these 7 subjects, 2 discontinued tenofovir alafenamide due to elevated amylase and/or lipase; 1 subject experienced recurrence of adverse events when tenofovir alafenamide was restarted. No subject treated with TDF had associated symptoms or discontinued treatment.

Serum Lipids

Changes from baseline in total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, and total cholesterol to HDL ratio among subjects treated with tenofovir alafenamide and TDF are presented in Table 4.

Table 4: Lipid Abnormalities: Mean Change from Baseline in Lipid Parameters in Patients with Chronic HBV Infection and Compensated Liver Disease in Studies 108 and 110 (Week 48 Analysis)

<table>
<thead>
<tr>
<th></th>
<th>Tenofovir Alafenamide (N=866)</th>
<th>TDF (N=432)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline mg/dL</td>
<td>Week 48 Change*</td>
<td>Baseline mg/dL</td>
</tr>
<tr>
<td>Total cholesterol (fasted)</td>
<td>188</td>
<td>0</td>
</tr>
</tbody>
</table>
### Overdosage

If overdose occurs, monitor patient for evidence of toxicity. Treatment of overdosage 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 hemodialysis with an extraction coefficient of approximately 54%.

### Shelf-Life

2 years from the date of manufacture

### Storage And Handling Instructions

TENVIR AF tablets containing 25 mg of tenofovir alafenamide are pink coloured, circular shape, biconvex, film coated tablets plain on both sides.

### Packaging Information

Each bottle contains 30 tablets, a silica gel desiccant, polyester coil, and is closed with a child resistant closure.

Last Updated: April 2018
Last Reviewed: April 2018

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TENVIR AF Tablets

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