GENTOVIR®

(Tenofovir Disoproxil Fumarate)
Tablets Ph.Int.

جینٹوور

۳۰۰ ملی گرام

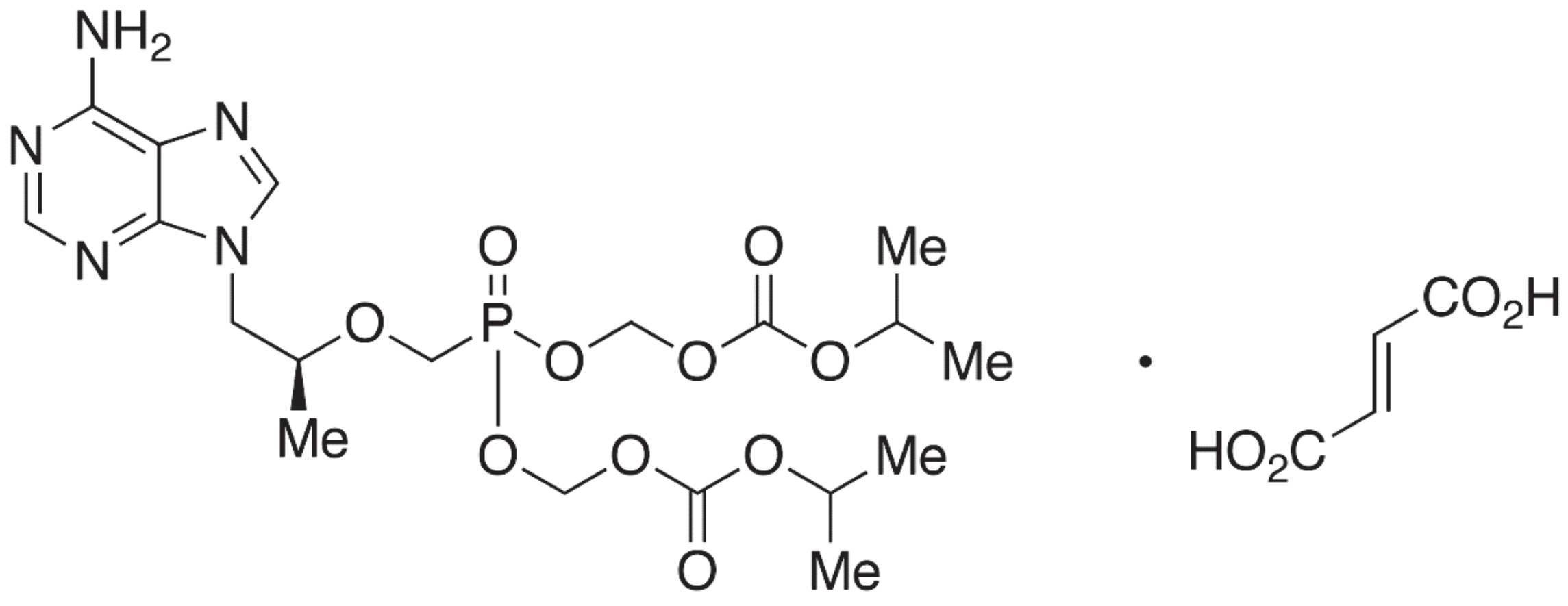
(ٹینوفوور ڈیسوپرکسل فیومریٹ) ٹیبلٹس انٹرنیشنل فارماکوپیا

300mg

DESCRIPTION:

GENTOVIR® is a prescription medicine used to treat chronic (long-lasting) hepatitis B virus (HBV) in people 12 years of age and older. The molecular formula is $C_{23}H_{34}N_5O_{14}P$ and the molecular weight is 635.5 g/mol.

Structure:



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

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 VIREAD.
- Severe acute exacerbations of hepatitis have been reported in HBV-infected patients who have discontinued anti-hepatitis B therapy, including VIREAD. Hepatic function should be monitored closely in these patients. If appropriate, resumption of anti-hepatitis B therapy may be warranted.

MECHANISM OF ACTION:

Tenofovir is taken up by cells and undergoes phosphorylation to the antivirally active metabolite PMPApp. PMPApp competitively inhibits both RNA- and DNA-directed reverse transcriptase activity. PMPApp competes with deoxyadenosine triphosphate (dATP) for incorporation into nascent DNA and, since it lacks a 3' hydroxyl group, causes premature chain termination. The Ki for reverse transcription (RNA-directed DNA synthesis) is 0.02 μM, more than 200-fold lower than the Ki for human DNA polymerase a, and more than 3,000-fold lower than the Ki values for β and γ. Generally, the lowest incorporation efficiencies with all three polymerases (α, β, and γ) were found for PMPApp when compared to ddATP, ddCTP, 3TCTP, d4TTP, or PMEGpp.

COMPOSITION:

Each film coated tablet contains:

Tenofovir Disoproxil Fumarate Ph.Int. .....300mg eq. to
Tenofovir Disoproxil 245mg

INDICATIONS:

GENTOVIR® is indicated in combination with other antiretroviral agents for the treatment of HIV infection in adults.

PHARMACOKINETICS:

Absorption The oral bioavailability of tenofovir from GENTOVIR® in fasted subjects is approximately 25%. The pharmacokinetics of tenofovir are dose proportional over a GENTOVIR® dose range of 75 to 600 mg and are not affected by repeated dosing.
Distribution In vitro binding of tenofovir to human plasma or serum proteins is less than 0.7 and 7.2%, respectively, over the tenofovir concentration range 0.01 to 25 μg/mL.
Metabolism and Elimination Following single dose, oral administration of GENTOVIR®, the terminal elimination half-life of tenofovir is approximately 17 hours. After multiple oral doses of GENTOVIR® 300 mg once daily (under fed conditions), 32 ± 10% of the administered dose is recovered in urine over 24 hours.
Effects of Food on Oral Absorption Administration of GENTOVIR® 300 mg tablets following a high-fat meal (~700 to 1000 kcal containing 40 to 50% fat) increases the oral bioavailability, with an increase in tenofovir AUC0–∞ of approximately 40% and an increase in Cmax of approximately 14%. Food delays the time to tenofovir Cmax by approximately 1 hour.

USE IN SPECIFIC POPULATIONS:

Pregnancy
Risk Category B:
no evidence of risk in humans.

Pediatric Patients: 2 Years of Age and Older: Steady-state pharmacokinetics of tenofovir were evaluated in 31 HIV-1 infected pediatric subjects 2 to less than 18 years. Tenofovir exposure achieved in these pediatric subjects receiving oral once daily doses of tenofovir disoproxil fumarate 300 mg (tablet) or 8 mg/kg of body weight (powder) up to a maximum dose of 300 mg was similar to exposures achieved in adults receiving once-daily doses of tenofovir disoproxil fumarate 300 mg.

CONTRAINDICATIONS:

GENTOVIR® (tenofovir disoproxil fumarate) is contraindicated in patients with previously demonstrated hypersensitivity to any of the components of the product.

WARNINGS AND PRECAUTIONS:

Lactic Acidosis and 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 , alone or in combination with other antiretrovirals.

Post-Treatment Exacerbation of Hepatitis:
Severe acute exacerbations of hepatitis have been reported in HBV-infected patients who have discontinued anti-hepatitis B therapy, including tenofovir disoproxil fumarate. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who discontinue anti-hepatitis B therapy, including tenofovir disoproxil fumarate. If appropriate, resumption of anti-hepatitis B therapy may be warranted.

Nephrotoxicity:
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 disoproxil fumarate during clinical practice.

SIDE EFFECTS:

The most common side effects of GENTOVIR® are Diarrhea, Nausea, Vomiting, Dizziness
Other side effects include Flatulence (intestinal gas), Allergic reaction, including angioedema (swelling of the blood vessels), with symptoms such as skin rash, redness, swelling of the hands, legs, feet, face, lips, tongue or throat with difficulty in breathing, Stomach pain, Weakness, Inflammation of the pancreas, Shortness of breath, Headache, Rash.

DRUG INTERACTIONS:

Avoid concomitant with other tenofovir disoproxil fumarate-containing products (eg, Atripla, Complera, Stribild, Truvada) or adefovir dipivoxil (eg, Hepsera). Avoid concomitant or recent use of nephrotoxic agents. Potentiates didanosine toxicity (reduce didanosine dose); discontinue if toxicity develops. Monitor drugs that reduce renal function or compete for renal tubular secretion (eg, cidofovir, acyclovir, valacyclovir, ganciclovir, valganciclovir). Potentiated by lopinavir/ritonavir, atazanavir + ritonavir, darunavir + ritonavir, ledipasvir/sofosbuvir; monitor for toxicity. Concomitant atazanavir: must give with ritonavir. Caution with triple nucleoside-only regimens (high rate of early viral non-response); monitor and consider alternative therapy.

OVERDOSE:

If overdose occurs the patient must be monitored for evidence of toxicity, and standard supportive treatment applied as necessary. Tenofovir is efficiently removed by hemodialysis with an extraction coefficient of approximately 54%. Following a single 300 mg dose of GENTOVIR®, a four-hour hemodialysis session removed approximately 10% of the administered tenofovir dose.

DOSAGE:

As directed by the physician.

INSTRUCTIONS:

Keep all medicines out of the reach of children.

STORAGE:

Store below 30°C.
Protect from heat, light & moisture.

HOW SUPPLIED:

GENTOVIR® (Tenofovir Disoproxil Fumarate) Tablets 300mg are available in Alu-Alu blister 3x10's pack.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایات: ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
روشنی، گرمی اور نمی سے محفوظ رکھیں۔ تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

For detailed information:

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