

hovid-Lamivudine Tablet

VILAMye-PC6 (MY)

DESCRIPTION

hovid-Lamivudine Tablet 150 mg

Oval, orange film-coated tablet, shallow convex "H" and "D" embossed on each side separated with a score line on the same face.

hovid-Lamivudine Tablet 300 mg

Caplet-shaped orange film-coated tablet, bevel-edged, shallow convex with break bar embossed on one face.

COMPOSITION

hovid-Lamivudine Tablet 150 mg

Lamivudine 150 mg per tablet

hovid-Lamivudine Tablet 300 mg

Lamivudine 300 mg per tablet

PHARMACODYNAMICS

Lamivudine belongs to a group of antiviral agents called nucleoside analogue reverse transcriptase inhibitors (NRTIs).

Lamivudine is converted intracellularly to the triphosphate derivative which is the active form of the parent compound. This triphosphate inhibits the DNA synthesis of retroviruses, including HIV, through competitive inhibition of reverse transcriptase and incorporation into viral DNA. Lamivudine is also active against hepatitis B virus.

PHARMACOKINETICS

Lamivudine is rapidly absorbed after oral doses and peak plasma concentrations occur in about 1 hour. Absorption is delayed, but not reduced, by ingestion with food. Bioavailability is between 80 and 87%. Binding to plasma protein is reported to be up to 36%. Lamivudine crosses the blood-brain barrier with a ratio of CSF to serum concentrations of about 0.12. It crosses the placenta and is distributed into breast milk.

Lamivudine is metabolized intracellularly to the active antiviral triphosphate. Hepatic metabolism is low and it is cleared mainly unchanged by active renal excretion. An elimination half-life of 5 to 7 hours has been reported after a single dose.

INDICATION

Lamivudine Tablet in combination with other anti-retroviral agents, is indicated for the treatment of human immunodeficiency virus (HIV) infected adults and children.

CONTRAINDICATIONS

Lamivudine is contraindicated in patients with hypersensitivity to the active substance or to any of the excipients.

WARNINGS AND PRECAUTIONS

- Lamivudine therapy should be stopped in patients who develop abdominal pain, nausea, or vomiting or with abnormal biochemical test results until pancreatitis has been excluded.
- Treatment with lamivudine may be associated with lactic acidosis and should be stopped if there is a rapid increase in aminotransferase concentrations, progressive hepatomegaly, or metabolic or lactic acidosis of unknown aetiology.
- Lamivudine should be used with caution in patients with hepatomegaly or other risk factors for hepatic disease.
- Patients co-infected with HIV and chronic hepatitis B or C and treated with combination antiretroviral therapy are at increased risk for severe and potentially fatal hepatic adverse events.

- Effect on driving and use machines:** No studies on the effects on the ability to drive and use machines have been performed.

PREGNANCY AND LACTATION

Pregnancy

There are no adequate and well-controlled studies of lamivudine tablets in pregnant women. Animal reproduction studies in rats and rabbits revealed no evidence of teratogenicity. Increased early embryolethality occurred in rabbits at exposure levels similar to those in humans. Lamivudine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Lactation

Lamivudine passes into breast milk. Because of the potential for serious adverse reactions in nursing infants and HIV-I transmission, mothers should be instructed not to breastfeed if they are receiving lamivudine.

DRUG INTERACTIONS

Renal excretion of lamivudine may be inhibited by other drugs mainly eliminated by active renal secretion, for example trimethoprim. Usual prophylactic doses of trimethoprim are unlikely to necessitate reductions in lamivudine dosage unless the patient has renal impairment, but the co-administration of lamivudine with the high doses of trimethoprim (as co-trimoxazole) used in pneumocystis pneumonia and toxoplasmosis should be avoided.

Although there is usually no clinically significant interaction with zidovudine, severe anemia has occasionally been reported in patients given lamivudine with zidovudine.

Lamivudine may antagonize the antiviral action of zalcitabine and the two drugs should not be used together.

In vitro lamivudine inhibits the intracellular phosphorylation of cladribine leading to a potential risk of cladribine loss of efficacy in case of combination in the clinical setting. Some clinical findings also support a possible interaction between lamivudine and cladribine. Therefore, the concomitant use of lamivudine with cladribine is not recommended.

Due to similarities, hovid-Lamivudine Tablet should not be administered concomitantly with other cytidine analogues, such as emtricitabine. Moreover, hovid-Lamivudine Tablet should not be taken with any other medicinal products containing lamivudine.

Once daily triple nucleoside regimens of lamivudine and tenofovir with either abacavir or didanosine are associated with a high level of treatment failure and of emergence of resistance, and should be avoided.

MAIN SIDE/ ADVERSE EFFECTS

Adverse effects commonly associated with lamivudine either as monotherapy or with other anti-retrovirals for the treatment of HIV include abdominal pain, nausea, vomiting, diarrhoea, headache, fever, rash, alopecia, malaise, insomnia, cough, nasal symptoms, arthralgia, and musculoskeletal pain.

There have also been reports of pancreatitis, anaemia, neutropenia, and thrombocytopenia. Increases in liver enzymes and serum amylase may occur. Lactic acidosis, usually associated with severe hepatomegaly and steatosis, has been reported during treatment with nucleoside reverse transcriptase inhibitors.

Immune reconstitution syndrome (an inflammatory immune response resulting in clinical deterioration) has been reported during the initial phase of treatment with combination antiretroviral therapy, including lamivudine, in HIV-infected patients with severe immune deficiency. Accumulation or redistribution of body fat (lipodystrophy) including central obesity, dorsocervical fat enlargement (buffalo hump), peripheral wasting, facial wasting, breast enlargement, and cushingoid appearance have been seen in patients receiving antiretroviral therapy, including lamivudine. Metabolic abnormalities such as hypertriglyceridaemia, hypercholesterolaemia, insulin resistance, hyperglycaemia, and hyperlactataemia have also been reported. NRTIs have also been associated with mitochondrial dysfunction manifesting as abnormal behavior, anaemia, convulsions, hyperlipasaemia, hypertonia, and neutropenia. Elevated creatine phosphokinase, myalgia, myositis, and rarely rhabdomyolysis have been reported, particular when nucleoside analogues have been given with HIV-protease inhibitors. Osteonecrosis has been reported, particularly in patients with advanced HIV disease or long term exposure to combination antiretroviral therapy.

Other side effects associated with combination antiretroviral therapy, including NRTIs may also occur.

OVERDOSE AND TREATMENT

Limited data are available on the consequences of ingestion of acute overdoses in humans. No fatalities occurred, and the patients recovered. No specific signs or symptoms have been identified following such overdose.

If overdose occurs the patient should be monitored and standard supportive treatment applied as required. Since lamivudine is dialyzable, continuous haemodialysis could be used in the treatment of overdose, although this has not been studied.

DOSAGE AND ADMINISTRATION

Lamivudine Tablet therapy should be initiated by a physician experienced in the management of HIV infection.

Oral. Lamivudine Tablet can be taken with or without food.

Adults, adolescents and children weighing at least 25 kg:

The recommended dose of Lamivudine Tablet is 300 mg daily. This may be administered as 150 mg twice daily or 300 mg once daily.

Children weighing 14 to < 20 kg:

The recommended oral dose of Lamivudine Tablet is either 75mg taken twice daily or 150mg taken once daily.

For children weighing ≥ 20 kg to <25 kg:

The recommended oral dose of Lamivudine Tablet is 75mg taken in the morning and 150mg taken in the evening.

Children weighing at least 25 kg:

The adult dosage of 150 mg twice daily or 300 mg once daily should be taken.

Children less than three months:

The limited data available are insufficient to propose specific dosage recommendations.

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Elderly:

No specific data are available. However, special care is advised in this age group due to age associated changes such as the decrease in renal function and alteration of haematological parameters.

Renal impairment:

Lamivudine plasma concentrations (AUC) are increased in patients with moderate to severe renal impairment due to decreased clearance. The dosage should therefore be reduced for patients with a creatinine clearance of less than 50 ml/min as shown in the table below. The same percentage reduction in dose applies for paediatric patients with renal impairment. When doses below 150 mg are required other suitable approved dosage form of lamivudine is recommended.

Dosing Recommendations - Adults, adolescents and children weighing at least 25 kg

Creatinine clearance (ml/min)	First Dose	Maintenance Dose
30 to less than 50	150 mg	150 mg once daily
15 to less than 30	150 mg	100 mg once daily
5 to less than 15	150 mg	50 mg once daily
less than 5	50 mg	25 mg once daily

Dosing Recommendations - Children aged more than 3 months and weighing less than 25 kg

Creatinine clearance (ml/min)	First Dose	Maintenance Dose
30 to less than 50	4 mg/kg	4 mg/kg once daily
15 to less than 30	4 mg/kg	2.6 mg/kg once daily
5 to less than 15	4 mg/kg	1.3 mg/kg once daily
less than 5	1.3 mg/kg	0.7 mg/kg once daily

Hepatic impairment:

No dose adjustment is necessary in patients with moderate or severe hepatic impairment unless accompanied by renal impairment.

Note: The information given here is limited. For further information, kindly consult your doctor or pharmacist.

Storage:

Store below 30°C.

Presentation/ Packing:

Blister pack of 1 x 10's, 3 x 10's, 10 x 10's.

Product Registration Holder: HOVID Bhd.

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Manufactured by: HOVID Bhd.

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