

Hivarif® (also known as 3TC) is the brand name for Lamivudine 150 mg Tablet and 100 ml (10 mg / ml) oral solution, a synthetic nucleoside analogue with activity against human immunodeficiency virus (HIV).

Presentation:

Hivarif® Tablet: Each film coated tablet contains Lamivudine USP 150 mg.

Hivarif® Oral Solution: Each ml solution contains Lamivudine USP 10 mg.

Pharmacology:

Intracellularly, Lamivudine is phosphorylated to its active 5'-triphosphate metabolite, Lamivudine triphosphate (L-TP). The principal mode of action of L-TP is the inhibition of HIV reverse transcriptase (RT) via DNA chain termination after incorporation of the nucleoside analogue into viral DNA. Lamivudine is rapidly absorbed after oral administration in HIV-infected patients. The majority of Lamivudine is eliminated unchanged in urine by active organic cationic secretion.

Indication:

Lamivudine in combination with other antiretroviral agents is indicated for the treatment of HIV infection.

Dosage & Administration:

Hivarif® may be administered with or without food.

Adults and adolescents over 12 years of age: the recommended dose of Hivarif® is 300 mg daily. This is administered as 150 mg twice daily.

Children: Three months to 12 years of age: the recommended dose is 4 mg/kg twice daily up to a maximum of 300 mg daily.

Less than three months of age: The limited data available are insufficient to propose specific dosage recommendations.

Dosage Adjustment:

Renal impairment: Lamivudine concentrations are increased in patients with moderate - severe renal impairment due to decreased clearance. The dose should therefore be adjusted.

Dosing Recommendations – Adults and adolescents over 12 years:

Creatinine Clearance First Dose Maintenance Dose
(ml/min)

50 150 mg 150 mg Twice daily

30- <50 150 mg 150 mg Once daily

15- 29 150 mg 100 mg Once daily

5- 14 150 mg 50 mg once daily

<5 50 mg 25 mg once daily

Hepatic Impairment: Data obtained in patients with moderate to severe hepatic impairment shows that Lamivudine pharmacokinetics are not significantly affected by

hepatic dysfunction. Based on these data, no dose adjustment is necessary in patients with moderate or severe hepatic impairment unless accompanied by renal impairment.

Contra-indication:

Hypersensitivity to Lamivudine or to any of the excipients.

Precaution & warning:

Lamivudin is not recommended for use as monotherapy.

In pediatric patients with a history of prior antiretroviral nucleoside exposure, a history of pancreatitis, or other significant risk factors for the development of pancreatitis, Lamivudine should be used with caution. Treatment with Lamivudine should be stopped immediately if clinical signs, symptoms, or laboratory abnormalities suggestive of pancreatitis occur

Lactic Acidosis/Severe Hepatomegaly with Steatosis: Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogues alone or in combination, including Lamivudine and other antiretrovirals. A majority of these cases have been in women. Obesity and prolonged nucleoside exposure may be risk factors. Particular caution should be exercised when administering Lamivudine to any patient with known risk factors for liver disease.

In patients with moderate to severe renal impairment, the dose should be adjusted. Patients receiving Lamivudin or any other antiretroviral therapy may continue to develop opportunistic infections and other complications of HIV infection, and therefore should remain under close clinical observation by physicians experienced in the treatment of patients with associated HIV diseases.

Adverse Effects:

The following adverse events have been reported during therapy for HIV disease with Lamivudine.

Blood and lymphatic systems disorders

Uncommon: Neutropenia, anaemia and thrombocytopenia

Very rare: Pure red cell aplasia

Nervous system disorders

Common: Headache, insomnia

Very rare: Cases of peripheral neuropathy (or paraesthesia).

Respiratory, thoracic and mediastinal disorders

Common: Cough, nasal symptoms

Gastrointestinal disorders

Common: Nausea, vomiting, abdominal pain or cramps, diarrhea

Rare: Rises in serum amylase. Cases of pancreatitis have been reported.

Hepatobiliary disorders

Uncommon: Transient rises in liver enzymes (AST, ALT).

Rare: Hepatitis

Skin and subcutaneous tissue disorders

Common: Rash, alopecia

Musculoskeletal and connective tissue disorders

Common: Arthralgia, muscle disorders

Rare: Rhabdomyolysis, Lipodystrophy

General disorders and administration site conditions

Common: Fatigue, malaise, fever.

Cases of lactic acidosis, usually associated with severe hepatomegaly and hepatic steatosis, have been reported with the use of nucleoside analogues.

Drug Interaction:

The possibility of interactions with other medicinal products administered concurrently should be considered, particularly when the main route of elimination is active renal secretion. Administration of trimethoprim/sulfamethoxazole 160 mg/800 mg results in a 40 % increase in Lamivudine exposure.

Lamivudine and zalcitabine may inhibit the intracellular phosphorylation of one another. Therefore, use of Lamivudine in combination with zalcitabine is not recommended.

Pregnancy and Lactation:

Pregnancy: Pregnancy Category C. The safety of Lamivudine in human pregnancy has not been established.

Lactation: Following oral administration Lamivudine excreted in breast milk at similar concentrations to those found in serum. That's why it is recommended that mothers taking Lamivudine do not breast-feed their infants.

Pharmaceutical Precaution:

Hivarif ® Tablet : Store in a cool and dry place, protect from light and moisture.

Hivarif ® Oral Solution : Store in a cool and dry place, protect from light.

How Supplied:

Hivarif ® Tablet : Each box contains 1 x 10 tablets in blister pack.

Hivarif ® Oral Solution : Each PET bottle contains 100 ml oral solution with a measuring cup and a calibrated dropper.