

COMPOSITION:

Avudin® is a combination tablet, containing Lamivudine and Zidovudine. Each film-coated tablet containing 150 mg of Lamivudine USP and 300 mg of Zidovudine BP.

PHARMACOLOGY:

Lamivudine and Zidovudine are synthetic nucleoside analogues with activity against human immunodeficiency virus (HIV).

Lamivudine: Intracellularly, Lamivudine is phosphorylated to its active 5'-triphosphate metabolite, Lamivudine triphosphate (L-TP). The principal mode of action of L-TP is inhibition of reverse transcription (RT) via DNA chain termination after incorporation of the nucleoside analogue. Following oral administration, Lamivudine is rapidly absorbed and extensively distributed. Binding to plasma protein is low.

Zidovudine: Intracellularly, Zidovudine is phosphorylated to its active 5'-triphosphate metabolite, Zidovudine triphosphate (ZDV-TP). The principal mode of action of ZDV-TP is inhibition of RT via DNA chain termination after incorporation of the nucleoside analogue. Following oral administration, Zidovudine is rapidly absorbed and extensively distributed. Binding to plasma protein is low. Zidovudine is eliminated primarily by hepatic metabolism.

Lamivudine Plus Zidovudine: Lamivudine in combination with Zidovudine (Avudin®) has synergistic antiretroviral activity. Synergistic activity of Lamivudine-Zidovudine was also shown in a variable ratio study.

INDICATION:

Avudin® is indicated for the treatment of HIV infection.

DOSAGE & ADMINISTRATION:

The recommended oral dose of Avudin® for adults and adolescents (at least 12 years of age) is 1 tablet (containing 150 mg of Lamivudine and 300 mg of Zidovudine) twice daily.

Dose Adjustment: As it is a fixed-dose combination, Avudin® should not be prescribed for patients requiring dosage adjustment such as those with reduced renal function (creatinine clearance <50 mL/min) or those experiencing dose-limiting adverse events or those with low body weight (< 50kg)

CONTRAINDICATION:

Avudin® Tablets are contraindicated in patients with previously demonstrated clinically significant hypersensitivity to any of the components of the product.

WARNINGS:

It is a fixed-dose combination of Lamivudine and Zidovudine. Ordinarily, this tablet should not be administered concomitantly with Lamivudine, Zidovudine, or a fixed-dose combination of abacavir, Lamivudine, and Zidovudine.

Bone Marrow Suppression: This tablet should be used with caution in patients who have bone marrow compromise evidenced by granulocyte count <1,000 cells/mm

3 or hemoglobin <9.5 g/dL. Frequent blood counts are strongly recommended in patients with advanced HIV disease who are treated with this tablet. For HIV-infected individuals and patients with asymptomatic or early HIV disease, periodic blood counts are 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 analogues alone or in combination, including Lamivudine, Zidovudine, 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 this preparation to any patient with known risk factors for liver disease or 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).

Myopathy: Myopathy and myositis, with pathological changes similar to that produced by HIV disease, have been associated with prolonged use of Zidovudine.

Post-treatment Exacerbations of Hepatitis: In clinical trials in non-HIV-infected patients treated with Lamivudine for chronic hepatitis B, clinical and laboratory evidence of exacerbations of hepatitis have occurred after discontinuation of Lamivudine. These exacerbations have been detected primarily by serum ALT elevations in addition to re-emergence of hepatitis B viral DNA (HBV DNA). Although most events appear to have been self-limited, fatalities have been reported in some cases. Similar events have been reported from post-marketing experience after changes from Lamivudine-containing HIV treatment regimens to non-Lamivudine-containing regimens in patients infected with both HIV and HBV. The causal relationship to discontinuation of Lamivudine treatment is unknown. Patients should be closely monitored with both clinical and laboratory follow-up for at least several months after stopping treatment. There is insufficient evidence to determine whether re-initiation of Lamivudine alters the course of posttreatment exacerbations of hepatitis.

PRECAUTION:

Patients with HIV and Hepatitis B virus Coinfection: Safety and efficacy of Lamivudine have not been established for treatment of chronic hepatitis B in patients dually infected with HIV and HBV. Emergence of hepatitis B virus variants associated with resistance to Lamivudine has also been reported in HIV-infected patients who have received

Lamivudine-containing antiretroviral regimens in the presence of concurrent infection with Hepatitis B virus. Post-treatment exacerbations of hepatitis have also been reported.

Patients with Impaired Renal Function: Reduction of the dosages of Lamivudine and Zidovudine is recommended for patients with impaired renal function. Patients with creatinine clearance <50 ml/min should not receive this combination tablet.

Fat Redistribution: Redistribution/accumulation of body fat including central obesity, dorsocervical fat enlargement (buffalo hump), peripheral wasting, facial wasting, breast enlargement, and cushingoid appearance have been observed in patients receiving antiretroviral therapy.

SIDE EFFECTS:

Side Effects of This Medicine-

More common

Chills, fever, pale skin; sore throat; unusual tiredness or weakness, headache

Less common

Abdominal pain, burning, tingling, numbness, or pain in the hands, arms, feet, or legs, muscle tenderness and weakness, nausea, skin rash, vomiting, yellow eyes or skin.

Coughing, decreased appetite, diarrhea, dizziness and trouble in sleeping may occur.

DRUG INTERACTION:

Lamivudine: Trimethoprim (TMP) 160 mg/ sulfamethoxazole (SMX) 800 mg once daily has been shown to increase Lamivudine exposure (AUC). The effect of higher doses of TMP/SMX on Lamivudine pharmacokinetics has not been investigated.

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

Zidovudine: Coadministration of ganciclovir, interferon-alpha, and other bone marrow suppressive or cytotoxic agents may increase the hematologic toxicity of Zidovudine.

Concomitant use of Avudin® with stavudine should be avoided since an antagonistic relationship with Zidovudine has been demonstrated in vitro. In addition, concomitant use of Zidovudine with doxorubicin or ribavirin should be avoided because an antagonistic relationship has been demonstrated in vitro.

USE IN PREGNANCY AND LACTATION:

Pregnancy Category C. There are no adequate and well-controlled studies of this drug in pregnant women. This drug should be used during pregnancy only if the potential benefits outweigh the risks.

The Centers for Disease Control and Prevention recommend that HIV-infected mothers should not breast-feed their infants to avoid risking postnatal transmission of HIV.

Because of the potential for HIV transmission and the potential for serious adverse effects in nursing infants, mothers should be instructed not to breast-feed if they are receiving efavirenz.

STORAGE CONDITION:

Avudin® Tablet should be stored at a cool and dry place, protected from light and moisture. Keep the medicine out of the reach of children.

HOW SUPPLIED:

Avudin® Tablet: Each box contains 1x10 tablets in blister pack.