Draft WHO Model Formulary (2007) entry for Zidovudine plus Lamivudine.

Source: http://mednet3.who.int/EMLib/modelFormulary/modelFormulary.asp

Name:

Zidovudine (Azidothymidine, AZT, ZDV)
PLUS
Lamivudine (3TC)

(Note: The abbreviation AZT, which has sometimes been used for zidovudine, has also been used for another drug).

Composition:

Each film coated tablet contains:

Zidovudine 300 mg
AND
Lamivudine 150 mg

Dose:

Zidovudine plus Lamivudine:
The recommended oral dose of the fixed dose combination for adults and adolescents (at least 12 years of age) is one tablet (containing 150 mg of lamivudine and 300 mg of zidovudine) twice daily with or without food.

Use:

Zidovudine and Lamivudine:
The indication is treatment of HIV infection, in combination with one or more additional antiretroviral drugs. Zidovudine and lamivudine belong to the nucleoside analogue class of antiretroviral drugs. Both drugs act by inhibiting the reverse transcriptase enzyme of HIV, and by terminating the growth of the DNA chain. Zidovudine and lamivudine in combination have been shown to have synergistic antiretroviral activity. However, they are not considered to be an effective treatment on their own and in practice should be combined with other nucleoside or non-nucleoside reverse transcriptase inhibitors, or with a protease inhibitor.

Contra-indications

The combination tablets are contraindicated in patients with previously demonstrated clinically significant hypersensitivity to any of the components of the product.

Precautions

Zidovudine
haematological toxicity; vitamin B12 deficiency (increased risk of neutropenia); reduce dose or interrupt treatment according to product literature if there is anaemia or myelosuppression; renal impairment (Appendix 4 of WHO Model Formulary); chronic hepatitis B or C, hepatic impairment (see Appendix 5 of WHO Model Formulary); risk of lactic acidosis, (see below); elderly; pregnancy and breastfeeding (see notes on pregnancy in the WHO model formulary); interactions: Appendix 1, WHO Model Formulary.

Hepatic Disease: Potentially life-threatening lactic acidosis and severe hepatomegaly with steatosis reported—caution in patients (particularly obese women) with hepatomegaly, hepatitis, liver enzyme abnormalities, or risk factors for liver disease and hepatic steatosis (including alcohol abuse); discontinue if rapid deterioration in liver function tests, symptomatic hyperlactataemia, progressive hepatomegaly or lactic acidosis

Lamivudine:
renal impairment (Appendix 4 of WHO Model Formulary), chronic hepatitis B or C, hepatic disease (see below); pregnancy and breastfeeding (see notes on pregnancy within the WHO model formulary); interactions: Appendix 1 of WHO Model Formulary.

Hepatic disease: Potentially life-threatening lactic acidosis and severe hepatomegaly with steatosis reported—caution in patients (particularly obese women) with hepatomegaly, hepatitis, liver enzyme abnormalities, or risk factors for liver disease and hepatic steatosis (including alcohol abuse); discontinue if rapid deterioration in liver function tests, symptomatic hyperlactataemia, progressive hepatomegaly or lactic acidosis. Recurrent hepatitis in patients with chronic hepatitis B may occur on discontinuation of lamivudine.

Adverse-effects:

Zidovudine:
anemia (may require transfusion), neutropenia, and leukopenia (all more frequent with high dose and advanced disease); also nausea and vomiting, abdominal pain, dyspepsia, diarrhoea, flatulence, taste disturbance, pancreatitis, liver disorders including fatty change and raised bilirubin and liver enzymes (see hepatic disease, above); chest pain, dyspnoea, cough; influenza-like symptoms, headache, fever, paraesthesia, neuropathy, convulsions, dizziness, somnolence, insomnia, anxiety, depression, loss of mental acuity, malaise, anorexia, asthenia, myopathy, myalgia; pancytopenia, thrombocytopenia; gynaecomastia; urinary frequency; rash, pruritus, pigmentation of nail, skin and oral mucosa.

Lamivudine:
nausea, vomiting, diarrhoea, abdominal pain; cough; headache, fatigue, insomnia; malaise, fever, rash, alopecia, muscle disorders; nasal symptoms; peripheral neuropathy reported; rarely pancreatitis (discontinue); neutropenia, anaemia, thrombocytopenia and red-cell aplasia; lactic acidosis; raised liver enzymes and serum amylase reported.