PRESCRIBING INFORMATION
Abacavir & Lamivudine Tablets

ABAKAST-L™

GENERIC NAME:
Abacavir & Lamivudine Tablets

COMPOSITION:
Each Film coated tablet contains
Abacavir Sulphate USP
equivalent to Abacavir 600mg
Lamivudine BP 300mg
Colour: Sunset yellow &Titanium Dioxide

PHARMACOLOGICAL ACTION:
Abacavir is a nucleoside analogue reverse transcriptase inhibitor. It is an antiviral agent against HIV-1 and HIV-2, including HIV-1 isolates that are resistant to zidovudine, lamivudine, zalcitabine, didanosine or nevirapine. *In vitro* studies have demonstrated that its mechanism of action in relation to HIV is inhibition of the HIV reverse transcriptase enzyme, an event that results in chain termination and interruption of the viral replication cycle.

PHARMACOKINETICS:
Absorption:
Abacavir is well absorbed following oral administration. The absolute bioavailability of oral abacavir in adults is about 83%. Following oral administration, the mean time (tmax) to maximal serum concentrations of abacavir is about 1,0 hour. Following oral administration, lamivudine is well absorbed with bioavailability of approximately 80%. The mean time (Tmax) to maximum serum concentration (Cmax) is about an hour. At therapeutic dose levels of 4 mg/kg/day (as two 12-hourly doses), Cmaxis in the order of 1-1.5 micrograms/mL. Food delayed absorption and decreased Cmax but did not affect overall plasma concentrations (AUC). Therefore abacavir can be taken with or without food.
Distribution:
Studies in HIV infected patients have shown good penetration of abacavir into the cerebrospinal fluid (CSF), with a CSF to plasma AUC ratio of between 30 to 44%.
In a phase I pharmacokinetic study, the penetration of abacavir into the CSF was investigated following administration of abacavir 300 mg twice a day. The mean concentration of abacavir achieved in the CSF 1,5 hours post dose was 0,14 micrograms/mL. The mean volume of distribution of lamivudine from intravenous studies has been reported as 1.3 L/kg and the mean terminal half-life of elimination as 5 to 7 hours.
In a further pharmacokinetic study of 600 mg twice a day, the CSF concentration of abacavir increased over time, from approximately 0,13 micrograms/mL at 0,5 to 1 hour after dosing, to approximately 0,74 micrograms/mL after 3 to 4 hours. While peak concentrations may not have been attained by 4 hours, the observed values are 9-fold greater than the IC50 of abacavir 0,08 micrograms/mL or 0,26 microM.
Metabolism:
Abacavir is primarily metabolised by the liver with less than 2% of the administered dose being renally excreted, as unchanged compound. The primary pathways of metabolism in man are by alcohol dehydrogenase and by glucuronidation to produce the 5'-carboxylic acid and 5'-glucuronide which account for about 66% of the dose in the urine. The mean systemic clearance of lamivudine is approximately 0.32 L/kg/h, with predominantly renal clearance of more than 70% via active tubular secretion, but little hepatic metabolism, at less than 10 L.
Elimination:
The mean half-life of abacavir is about 1,5 hoursElimination of abacavir is via hepatic metabolism with subsequent excretion of metabolites primarily in the urine. The metabolites and unchanged abacavir account for about 83% of the administered abacavir dose in the urine, the remainder is eliminated in the faeces. The intracellular half-life of the lamivudine triphosphate active metabolite is prolonged, averaging over 10 hours in peripheral blood lymphocytes.
WARNING:
Hypersensitivity: In clinical studies, approximately 4% of subjects receiving Abacavir developed a hypersensitivity reaction which in rare cases proved fatal.Patients receiving LAMIVUDINE and other antiretroviral agents may continue to develop opportunistic infections and other complications of HIV infection.
Description: This is characterised by the appearance of symptoms indicating multiorgan/body-system involvement. The majority of patients have fever and/or rash as part of the syndrome. The symptoms of this hypersensitivity reaction can occur at any time during treatment with Abacavir & Lamivudine, but usually appear within the first 6 weeks of initiation of treatment with Abacavir (median time to onset 11 days), and most often include fever, gastrointestinal symptoms (nausea, vomiting, diarrhoea and abdominal pain), rash and fatigue or malaise. Other symptoms may include myalgia, arthralgia, oedema, paraesthesia and respiratory symptoms such as dyspnoea, sore throat or cough. Prescribers must ensure that patients are fully informed regarding the following hypersensitivity reaction:

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of lamivudine alone or in combination, in the treatment of HIV infection.

DOSAGE AND DIRECTIONS FOR USE:
Abacavir should be prescribed by physicians experienced in the management of HIV infection.
To ensure administration of the entire dose, the tablet(s) should ideally be swallowed without crushing.
Adults and adolescents (over 12 years of age): the recommended dose of Abacavir is 600 mg once daily. The recommended dose of Lamivudine is 300 mg once daily.
Children (under 12 years of age):A dosing according to weight bands is recommended for Abacavir tablets. This dosing regimen for paediatric patients weighing 14-30 kg is based primarily on pharmacokinetic modeling.The recommended dose for Lamivudine is 4 mg/kg twice daily upto a maximum of 300 mg daily.
Children weighing at least 30 kg: the adult dosage of 300 mg twice daily should be taken. For patients with low body weights (less than 50 kg), the recommended oral dose of LAMIVUDINE is 2 mg/kg twice daily.
Children weighing > 21 kg to < 30 kg: one half of a Abacavir & lamivudine tablet taken in the morning and one whole tablet taken in the evening.
Children less than three months: the experience in children aged less than three months is limited
Children <3 months of age: There are limited data to propose specific dosage recommendations.

SIDE EFFECTS AND SPECIAL PRECAUTIONS
Side-effects:The signs and symptoms of this hypersensitivity reaction are listed below.

Blood and the lymphatic system disorders:
Less frequent (incidence approximately 5%):Abacavir causes , lymphadenopathy, lymphopenial. Neutropenia, thrombocytopenia and anaemia have occurred with Lamivudine.
Nervous system disorders:
Less frequent (incidence approximately 5%): paraesthesia
Eye disorders:
Less frequent (incidence approximately 5%): conjunctivitis
Cardiac disorders:
Less frequent (incidence approximately 5%): hypotension
Vascular disorders:
Less frequent (incidence approximately 5%): headache

Pancreatitis: Pancreatitis has been observed in some patients receiving Lamivudine. However it is unclear whether this is due to LAMIVUDINE or to underlying HIV disease.
Lactic acidosis/severe hepatomegaly with steatosis: Long-term use of LAMIVUDINE can result in potentially fatal lactic acidosis. Symptomatic hyperlactacaemia and lactic acidosis are uncommon. Clinical features are non-specific, and include nausea, vomiting, abdominal pain, dyspnoea, fatigue and weight loss.

KNOWN SYMPTOMS OF OVERDOSAGE AND

PARTICULARS OF ITS TREATMENT:
Single doses up to 1200 mg and daily doses up to 1800 mg of abacavir have been administered to patients in clinical studies. It is not known whether abacavir can be removed by peritoneal dialysis or haemodialysis. Treatment is symptomatic and supportive for Lamivudine.

SHELF LIFE Refer Label for the Shelf Life..

PRESENTATION: 30 Tablets pack in HDPE bottle & is packed in an individual carton along with a package insert.

STORAGE INSTRUCTIONS:
Store below 30ºC. Protect from light.
KEEP OUT OF REACH OF CHILDREN.

MARKETED BY:

APRAZER

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