Lamivudine (Epivir®, 3TC)

Class:
Lamivudine is a nucleoside analogue.

Antiviral Activity:
Lamivudine has activity against HIV-1, HIV-2 and hepatitis B virus.

Mechanism of Action:
Lamivudine must be converted intracellularly to its triphosphate form, which then competes with cytosine triphosphate for incorporation into the developing viral DNA strand. This results in chain termination and ceases viral DNA replication.

Mechanism of Resistance:
Resistance to NRTIs occurs through two mechanisms; decreased incorporation of NRTIs into the viral DNA and increased excision of NRTIs from the viral DNA.

Pharmacokinetics:
Lamivudine tablets, capsules, and oral solution dosage forms are bioequivalent. Protein binding is less than 36%. Approximately 5% is recovered in the urine as a trans-sulfoxide metabolite and 70% is excreted unchanged in the urine. Active tubular secretion appears to play a role in the clearance.

Adverse Effects:
The most common side effects are nausea, diarrhea and headache. Peripheral neuropathy, myalgias, pancreatitis, and lactic acidosis occur infrequently.

Dosage:
Tablet 150mg, 300mg
Oral Solution 10mg/ml

HIV-1 – 150 mg orally every 12 hours
HBV – 100 mg orally once daily

Disease state based dosing:
Renal Impairment:
CrCl =50 ml/min:
    HIV-1 – 150mg twice daily or 300mg once daily
    HBV – 100mg once daily
CrCl 30-49 ml/min:
    HIV-1 – 150mg once daily
    HBV – 100mg x one dose then 50mg once daily
CrCl 15-29 ml/min
    HIV-1 – 150mg x one dose then 100mg once daily
    HBV – 100mg x one dose then 25mg once daily

CrCl 5-14 ml/min

HIV-1 – 150mg x one dose then 50mg once daily

HBV – 35mg x one dose then 15mg once daily

CrCl < 5 ml/min

HIV-1 – 50mg x one dose then 25mg once daily

HBV – 35mg x one dose then 10mg once daily

Hepatic Impairment:
No dose adjustment necessary

Contraindications/Warnings/ Precautions:
Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of NRTIs. Use with caution in pediatric patients who are at risk for the development of pancreatitis.

Drug Interactions:
Zalcitabine – lamivudine and zalcitabine may result in mutual inhibition of intracellular phosphorylation.

Pregnancy:
Category C: Risk unknown. Human studies inadequate.

Monitoring Requirements:
LFTs, serum creatinine/BUN

Brand names/Manufacturer:
Epivir®/GlaxoSmithkline