Front

Tacavir®

(Entecavir)

Tablet

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COMPOSITION:

Tacavir Tablet 0.5 mg:

Each film coated tablet contains:
Entecavir Monohydrate equivalent to
Entecavir ..... 0.5 mg.

Product Specs.: CCL Pharmaceuticals

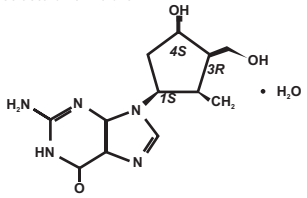
Tacavir Tablet 1 mg:

Each film coated tablet contains:
Entecavir Monohydrate equivalent to
Entecavir ..... 1 mg.

Product Specs.: CCL Pharmaceuticals

DESCRIPTION:

Tacavir (Entecavir) is a guanosine nucleoside analogue with selective activity against hepatitis B virus (HBV). The chemical name for Entecavir is 2-amino-1,9-dihydro-9-[(1S,3R,4S)-4-hydroxy-3-(hydroxymethyl)-2-methylenecyclopentyl]-6 H-purin-6-one, monohydrate. Its molecular formula is $C_{12}H_{15}N_5O_3 \cdot H_2O$, molecular weight 295.299. and its Structural formula is.



MICROBIOLOGY:

Entecavir triphosphate functionally inhibits all three activities of the HBV polymerase (reverse transcriptase, rt): (1) base priming, (2) reverse transcription of the negative strand from the pregenomic messenger RNA, and (3) synthesis of the positive strand of HBV DNA. Entecavir triphosphate is a weak inhibitor of cellular DNA polymerases α, β, and ∂ and mitochondrial DNA polymerase g with Ki values ranging from 18 to >160 μM.

Antiviral activity:

Entecavir inhibited HBV DNA synthesis (50% reduction, EC50) at a concentration of 0.004 μM in human HepG2 cells transfected with wild-type HBV. The median EC50 value for entecavir against lamivudine-resistant HBV (rtL180M, rtM204V) was 0.026 μM (range 0.010–0.059 μM). The coadministration of HIV nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) with entecavir is unlikely to reduce the antiviral efficacy of entecavir against HBV or of any of these agents against HIV.

Resistance:

In cell culture: 8- to 30-fold reductions in entecavir phenotypic susceptibility were observed for lamivudine-resistant strains.

Cross-resistance has been observed among HBV nucleoside analogues. In cell-based assays, entecavir had 8- to 30-fold less inhibition of HBV DNA synthesis for HBV containing lamivudine and telbivudine resistance substitutions rtM204I/V with or without rtL180M than for wild-type HBV.

PHARMACOKINETICS:

Absorption: The bioavailability of the tablet was 100% relative to the oral solution. entecavir peak plasma concentrations occurred between 0.5 and 1.5 hours. Following multiple daily doses ranging from 0.1 to 1.0 mg, Cmax and area under the concentration-time curve (AUC) at steady state increased in proportion to dose. The estimated apparent volume of distribution is in excess of total body water, suggesting that entecavir is extensively distributed into tissues. Binding of entecavir to human serum proteins in vitro was approximately 13%.Minor amounts of phase II metabolites (glucuronide and sulfate conjugates) were observed. Entecavir is not a substrate, inhibitor, or inducer of the cytochrome P450 (CYP450) enzyme system. Entecavir is predominantly eliminated by the kidney.

Special Populations:

Gender: There are no significant gender differences in entecavir pharmacokinetics.

Race: There are no significant racial differences in entecavir pharmacokinetics.

Elderly: Entecavir AUC was 29.3% greater in elderly subjects compared to young subjects.

Pediatrics: Pharmacokinetic studies have not been conducted in children.

Hepatic impairment: No pharmacokinetics differences, no dosage adjustment of BARACLUDE is recommended for patients with hepatic impairment.

Renal impairment: oral clearance of entecavir decreased as creatinine clearance decreased Dosage adjustment is recommended for patients with creatinine clearance less than 50 mL/min, including patients on hemodialysis or continuous ambulatory peritoneal dialysis (CAPD)

INDICATIONS AND USAGE:

Tacavir (Entecavir) is indicated for the treatment of chronic hepatitis B virus infection in adults with evidence of active viral replication and either evidence of persistent elevations in serum aminotransferases (ALT or AST) or histologically active disease.

DOSAGE AND ADMINISTRATION:

TACAVIR (Entecavir) should be administered on an empty stomach (at least 2 hours after a meal and 2 hours before the next meal). ***Compensated Liver Disease:***

For chronic hepatitis B virus infection in nucleosidetreatment-naïve adults and adolescents 16 years of age and older is 0.5 mg once daily.

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Decompensated liver disease:

For chronic hepatitis B virus infection in adults with decompensated liver disease is 1 mg once daily. The recommended dose of TACAVIR in adults and adolescents (at least 16 years of age) with a history of hepatitis B viremia while receiving lamivudine or known lamivudine or telbivudine resistance mutations rtM204I/V with or without rtL180M, rtL80I/V, or rtV173L is 1 mg once daily.

Renal impairment: Oral clearance of entecavir decreased as creatinine clearance decreased. Dosage adjustment is recommended for patients with creatinine clearance less than 50 mL/min, including patients on hemodialysis or continuous ambulatory peritoneal dialysis (CAPD).

Duration of therapy: The optimal duration of treatment with TACAVIR for patients with chronic hepatitis B virus infection and the relationship between treatment and long-term outcomes such as cirrhosis and hepatocellular carcinoma are unknown.

CONTRAINDICATIONS:

Tacavir (Entecavir) is contraindicated in patients with hypersensitivity to Entecavir or any component of the product.

WARNINGS AND PRECAUTIONS:

Severe acute exacerbations of hepatitis B have been reported in patients who have discontinued anti-hepatitis B therapy, including entecavir. Hepatic function should be monitored closely for several months in patients who discontinue anti-hepatitis B therapy.

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogues, including Tacavir. Treatment with Tacavir should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity.

Pregnancy Category C:

Tacavir should be used during pregnancy only if clearly needed and after careful consideration of the risks and benefits.

Nursing mothers: It is not known whether TACAVIR is excreted into human milk.but should be use cautiously.

Pediatric use: Safety and effectiveness of entecavir in pediatric patients below the age of 16 years have not been established.

ADVERSE REACTIONS:

The most common adverse events were headache, fatigue, dizziness, and nausea.

Gastrointestinal: Diarrhea, Dyspepsia, Nausea, Vomiting, Fatigue.

Nervous System: Headache, Dizziness, Somnolence.

Psychiatric: Insomnia, Includes events of possible, probable, certain, or unknown relationship to treatment regimen.

DRUG INTERACTIONS:

Co-administration of Entecavir with lamivudine, adefovir dipivoxil, or tenofovir disoproxil fumarate did not result in significant drug interactions. The effects of coadministration of Tacavir (Entecavir) with other drugs that are renally eliminated or are known to affect renal function have not been evaluated, and patients should be monitored closely for adverse events when Tacavir (Entecavir) is co-administered with such drugs.

OVERDOSAGE:

There is limited experience of entecavir overdosage reported in patients. If overdose occurs, the patient must be monitored for evidence of toxicity, and standard supportive treatment applied as necessary. A 4-hour hemodialysis session removed approximately 13% of the entecavir dose.

INSTRUCTIONS:

- Store below 30°C.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:

Tacavir Tablet 0.5 mg	:	Pack of 3 x 10 tablets.
Tacavir Tablet 1 mg	:	Pack of 3 x 10 tablets.

ہدایات:

۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف ڈاکٹر کے نسخہ پر فروخت کریں۔

FOR FURTHER INFORMATION PLEASE CONTACT:

Manufactured by:
CCL Pharmaceuticals (Pvt.) Ltd.
62 Industrial Estate, Kot Lakhpat, Lahore, Pakistan.

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