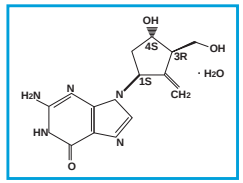
PRESCRIBING INFORMATION

CAVIRA® 0.5mg Tablets
(Entecavir)

کویرا 0.5 ملی گرام ٹیبلٹس

COMPOSITION
Each film coated tablet contains:
Entecavir……Brookes Specs…. 0.5mg
(as monohydrate)
Mfg. Specs. Brookes

DESCRIPTION
Cavira (Entecavir), a guanosine nucleoside analogue with selective activity against HBV. Its molecular formula is $C_{12}H_{15}N_5O_3 \cdot H_2O$, which corresponds to a molecular weight of 295.3. Cavira (Entecavir) has the following structural formula:



CLINICAL PHARMACOLOGY
Cavira (Entecavir) 0.5mg tablet, a guanosine nucleoside analogue with activity against HBV polymerase, is efficiently phosphorylated to the active triphosphate form, which has an intracellular half-life of 15 hours. By competing with the natural substrate deoxyguanosine triphosphate, entecavir triphosphate functionally inhibits all three activities of the HBV polymerase (reverse transcriptase, (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.

PHARMACOKINETICS
Absorption:
Following oral administration of Cavira (Entecavir) 0.5mg tablet, peak plasma concentrations occurred between 0.5 and 1.5 hours. Cmax and area under the concentration-time curve (AUC) at steady state increased in proportion to dose. Steady state was achieved after 6 to 10 days of once-daily administration with approximately 2-fold accumulation. Food resulted in a delay in absorption.

Distribution
Cavira (Entecavir) 0.5mg tablet has an estimated apparent volume of distribution is in excess of total body water, suggesting that Cavira (Entecavir) is extensively distributed into tissues. Protien binding of Cavira(Entecavir) was approximately 13%.

Metabolism and Elimination
Cavira (Entecavir) 0.5mg tablet is not a substrate, inhibitor, or inducer of the cytochrome P450 (CYP450) enzyme system. After reaching peak concentration, Cavira (Entecavir) 0.5mg tablet plasma concentrations decreased in a bi-exponential manner with a terminal elimination half-life of approximately 128-149 hours. The observed drug accumulation index is approximately 2-fold with once-daily dosing, suggesting an effective accumulation half-life of approximately 24 hours.

Cavira (Entecavir) 0.5mg tablet is predominantly eliminated by the kidney with urinary recovery of unchanged drug at steady state ranging from 62% to 73% of the administered dose. Renal clearance is independent of dose and ranges from 360 to 471 ml/min suggesting both glomerular filtration and net tubular secretion.

Dosage adjustment of Cavira (Entecavir) should be based on the renal function of the patient. No dosage adjustment of Cavira (Entecavir) is recommended for patients with hepatic impairment. Pharmacokinetic studies have not been conducted in children.

INDICATIONS
Cavira (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. The following points should be considered when initiating therapy with Cavira (Entecavir) tablet.

• The indication is based on histologic, virologic, biochemical, and serologic responses in nucleoside-treatment-naive and lamivudine-resistant adult subjects with HBeAg-positive or HBeAg-negative chronic HBV infection with compensated liver disease.

• Limited data are available in adult subjects with HIV/HBV co-infection who have received prior lamivudine therapy. Cavira (Entecavir)has not been evaluated in patients with decompensated liver disease.

DOSAGE & ADMINISTRATION
Cavira (Entecavir) should be administered on an empty stomach (at least 2 hours before a meal). The recommended dose of Cavira (Entecavir) for chronic hepatitis B virus infection in nucleoside-treatment-naive adults and adolescents 16 years of age and older is 0.5 mg once daily. The recommended dose of Cavira (Entecavir) in adults and adolescents (at least 16 years of age) with a history of hepatitis B viremia while receiving lamivudine or telbivudine) is 1 mg once daily.

Dosage Adjustment in Renal Impairment:
In subjects with renal impairment, the apparent oral clearance of Cavira (Entecavir) is 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), as shown in Table . The once-daily dosing regimens are preferred.

Recommended Dosage of Entecavir in Patients with Renal Impairment

If administered on a hemodialysis day, administer Cavira (Entecavir) after the Hemodialysis session.

Creatinine Clearance (ml/min)	Usual Dose (0.5 mg)	Lamivudine- Refractory
⩾ 50	0.5 mg once daily	1 mg once daily
30 to < 50	0.25 mg once daily or 0.5 mg every 48 hours	0.5 mg once daily or 1 mg every 48 hours
10 to < 30	0.5 mg every 72 hours	1 mg every 72 hours
< 10 Hemodialysis or CAPD	0.5 mg every 7 days	1 mg every 7 days

SIDE EFFECTS

Cavira (Entecavir) is very well tolerated drug exhibiting low side effect profile. Most common adverse reactions are (=3%, all severity grades) are headache, fatigue, dizziness, and nausea. Less common side effects include diarrhea, indigestion, vomiting, sleepiness, and trouble sleeping. There have also been occasional reports of rash. In some patients, the results of blood tests that measure how the liver or pancreas is working may worsen. Cavira (Entecavir) may cause the following serious side effects if stop taking the drug immediately

• A worse or very serious hepatitis.
• Lactic acidosis and liver problems.

CONTRA-INDICATIONS

Cavira (Entecavir) is contra-indicated in those who have hypersensitivity reaction with the active ingredient of the drug

DRUG INTERACTIONS

The pharmacokinetics of Cavira (Entecavir) is unlikely to be affected by co-administration with agents that are either metabolized by, inhibit, or induce the CYP450 system.

USE IN SPECIAL SITUATIONS

Pregnancy:

There are no adequate and well-controlled studies of Cavira (Entecavir) in pregnant women. Cavira (Entecavir) should be used during pregnancy only if clearly needed and after careful consideration of the risks and benefits. No data on the effect of Cavira (Entecavir) on transmission of HBV from mother to infant.

Nursing Mothers:

It is not known whether Cavira (Entecavir) is excreted into human milk. A decision should be made to discontinue nursing or to discontinue Cavira (Entecavir) taking into consideration the importance of continued hepatitis B therapy to the mother and the known benefits of breastfeeding.

Pediatric patients:

Safety and effectiveness of Cavira (Entecavir) in pediatric patients below the age of 16 years have not been established.

Geriatric Patients:

Cavira (Entecavir) is substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

INFORMATION ABOUT TREATMENT

Physicians should inform their patients of the following important points when initiating Cavira (Entecavir) 0.5mg tablets treatment:

• Patients should remain under the care of a physician while taking Cavira (Entecavir) 0.5mg tablets. They should discuss any new symptoms or concurrent medications with their physician.

•Patients should be advised that treatment with Cavira (Entecavir) 0.5mg tablets has not been shown to reduce the risk of transmission of HBV to others through sexual contact or blood contamination.

• Patients should be advised to take Cavira (Entecavir) 0.5mg tablets on an empty stomach (at least 2 hours before the meal).

STORAGE

Store at temperature 15 to 30 ºC, away from light & moisture.

PRESENTATION

Cavira (Entecavir) is available in Alu Alu blister pack of 30 Tablets.

خوراک اور طریقہ استعمال:

کویرا (اینٹی کویر) 0.5 ملی گرام ٹیبلیٹ خالی پیٹ (کھانے سے کم از کم 2 گھنٹے پہلے) لینی چاہیے۔

کویرا 0.5 ملی گرام ٹیبلیٹ کو معروضی ہیپاٹائٹس B وائرل انفیکشن سولہ سال (16) سے بڑی عمر میں ایک گولی روزانہ دینی چاہیے۔

16 سال سے بڑی عمر کے وہ مریض جن کو ہیپاٹائٹس B وائرس کی دوسری ادویات دی گئی ہوں ان کو (۱) ایک ملی گرام خوراک دینی چاہیے۔

اسٹوریج:

15 سے 30 ڈگری سینٹی گریڈ درجہ حرارت پر روشنی اور نمی سے بچا کر رکھیے۔

brookes
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