Entecavir PK Fact Sheet

Details

Generic Name Entecavir
Trade Name Baraclude®
Class Guanosine nucleoside analogue with selective antiviral activity against HBV polymerase
Molecular Weight 295.3
Structure

Summary of Key Pharmacokinetic Parameters

Entecavir is phosphorylated to the active triphosphate form, which has an intracellular half-life of 15 hours.

Linearity/non-linearity Dose-proportionate increases in Cmax and AUC following multiple doses ranging from 0.1-1 mg.

Steady state Achieved between 6-10 days after once daily dosing with ~2 times accumulation.

Plasma half life When peak levels reached, terminal elimination half-life is approx. 128-149 hours.

Cmax 4.2 ng/ml (0.5 mg dose) at steady state
8.2 ng/ml (1 mg dose) at steady state

Cmin 0.3 ng/ml (0.5 mg dose) at steady state
0.5 ng/ml (1 mg dose) at steady state

AUC 27.9 ng.h/ml (1 mg single dose)

Bioavailability Absolute bioavailability not determined; estimated to be at least 70%.

Absorption Administration with a high fat or light meal results in slight delay in absorption; a 44-46% decrease in Cmax, and an 18-20% decrease in AUC. The US Prescribing Information recommends that all patients should take entecavir on an empty stomach (at least 2 hours after a meal and 2 hours before the next meal), but the European SmPC only makes this recommendation for lamivudine-refractory patients and those with decompensated liver disease.

Protein Binding Approximately 13% in vitro

Volume of Distribution Estimated to be in excess of total body water

CSF:Plasma ratio Data unavailable

Semen:Plasma ratio Data unavailable

Renal Clearance 75% of dose as unchanged drug, at steady state. Thought to undergo both glomerular filtration and net tubular secretion.

Renal Impairment Clearance of entecavir decreases with decreasing creatinine clearance. The manufacturer recommends dose adjustment with creatinine clearance <50 ml/min, including those on haemodialysis or continuous ambulatory peritoneal dialysis. A 4-hour period of haemodialysis removed ~13% of the dose, and 0.3% was removed by CAPD. On haemodialysis days, administer entecavir after haemodialysis. Virological response should be closely monitored.

Hepatic Impairment Pharmacokinetics in moderate or severe hepatic impairment are similar to those in normal hepatic function. The European SmPC states that dosage adjustments are not necessary. The...
US Prescribing Information states that the recommended dose in adults with decompensated liver disease is 1 mg once daily.

**Metabolism and Distribution**

**Metabolised by**
- Not a substrate for CYP450.
- No acetylation or oxidation; minor phase II glucuronidation and sulphate conjugation.

**Inducer of**
- Not an inducer of CYP450

**Inhibitor of**
- Not an inhibitor of CYP450

**Transported by**
- Data unavailable

**References**

All information is from:
- Baraclude® Summary of Product Characteristics, Bristol-Myers Squibb Pharmaceuticals Ltd.
- Baraclude® US Prescribing Information, Bristol-Myers Squibb.