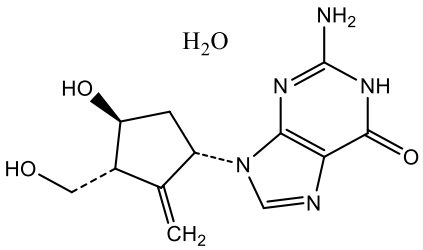
Entecavir PK Fact Sheet

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.