Elbasvir PK Fact Sheet

Details

Generic Name  Elbasvir
Trade Name  Zepatier® (co-formulated with grazoprevir)
Class  HCV NS5A inhibitor
Molecular Weight  882.02
Structure

Summary of Key Pharmacokinetic Parameters

Elbasvir is available in a fixed-dose combination product with grazoprevir.

Linearity/non-linearity  Elbasvir pharmacokinetics were approximately dose-proportional over the range of 5-100 mg once daily.
Steady state  Achieved after approximately 6 days of once daily dosing.
Plasma half life  ~ 24 h
Cmax  121 (118, 123) ng/ml (mean, 90% CI, based on population PK modelling)
C24  48.4 (47.3, 49.6) ng/ml (mean, 90% CI, based on population PK modelling)
AUC  1920 (1880, 1960) ng.h/ml (mean, 90% CI, based on population PK modelling)
Bioavailability  Not determined
Absorption  Relative to fasting conditions, the administration of a single dose of elbasvir/grazoprevir with a high-fat (900 kcal, 500 kcal from fat) meal to healthy subjects decreased elbasvir AUC and Cmax by approximately 11% and 15%, respectively. These differences in exposure are not clinically relevant; therefore, elbasvir/grazoprevir may be taken without regard to food.
Protein Binding  >99.9%
Volume of Distribution  680 L (based on population PK modelling)
CSF:Plasma ratio  Not determined
Semen:Plasma ratio  Not determined
Renal Clearance  <1%
Renal Impairment  No dosage adjustment of elbasvir/grazoprevir is recommended in patients with any degree of renal impairment including patients on haemodialysis. Elbasvir is not removed by haemodialysis and is unlikely to be removed by peritoneal dialysis as it is highly protein bound.
Hepatic Impairment  No dosage adjustment of elbasvir/grazoprevir is recommended in patients with mild hepatic impairment (Child-Pugh A). Elbasvir/grazoprevir is contraindicated in patients with moderate or severe hepatic impairment (Child-Pugh B or C) due to the expected significantly increased grazoprevir plasma concentration (a 12-fold increase in grazoprevir exposure was observed in non-HCV infected Child-Pugh C subjects) and the increased risk of alanine aminotransferase (ALT) elevations.
Elbasvir PK Fact Sheet

Metabolism and Distribution

Metabolised by CYP3A
Inducer of Unlikely to induce CYP1A2, CYP2B6, CYP3A.
Inhibitor of Inhibits P-gp and BCRP. Does not inhibit CYP3A.
No clinically significant inhibition of CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, and CYP2D6,
UGT1A1, and esterases (CES1, CES2, and CatA) expected.
Transported by P-gp

References

Unless otherwise stated (see below), information is from:
Zepatier® US Prescribing Information, Merck & Co Inc.