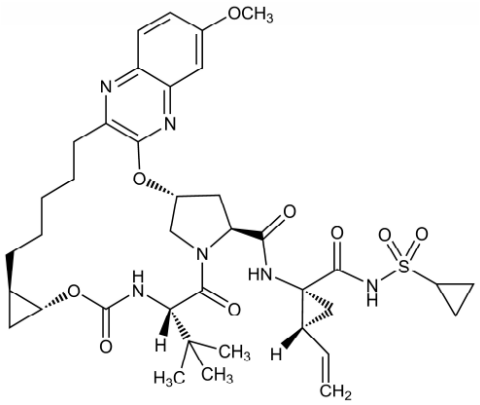
Grazoprevir PK Fact Sheet

Details

Generic Name	Grazoprevir
Trade Name	Zepatier® (co-formulated with elbasvir)
Class	HCV NS3/4A protease inhibitor
Molecular Weight	766.90
Structure	

Summary of Key Pharmacokinetic Parameters

Grazoprevir is available in a fixed-dose combination product with elbasvir.

Linearity/non-linearity	Grazoprevir pharmacokinetics increased in a greater than dose-proportional manner over the range of 10-800 mg once daily in HCV-infected subjects.
Steady state	Achieved after approximately 6 days of once daily dosing.
Plasma half life	~31 h
Cmax	165 (161, 176) ng/ml (mean, 90% CI, based on population PK modelling)
C24	18.0 (17.8, 19.9) ng/ml (mean, 90% CI, based on population PK modelling)
AUC	1420 (1400, 1530) 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 increased grazoprevir AUC and Cmax by approximately 1.5-fold and 2.8-fold, respectively. These differences in exposure are not clinically relevant; therefore, elbasvir/grazoprevir may be taken without regard to food.
Protein Binding	>98.8%
Volume of Distribution	1250 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. Grazoprevir 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.

Metabolism and Distribution

Metabolised by	CYP3A
Inducer of	Unlikely to induce CYP1A2, CYP2B6, CYP3A.
Inhibitor of	Inhibits BCRP. Weak inhibitor of CYP3A. Does not inhibit P-gp. No clinically significant inhibition of CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, and CYP2D6, UGT1A1, and esterases (CES1, CES2, and CatA) expected.
Transported by	OATP1B1/3, P-gp

References

Unless otherwise stated (see below), information is from:

Zepatier® Summary of Product Characteristics, Merck Sharp & Dohme Ltd.
Zepatier® US Prescribing Information, Merck & Co Inc.