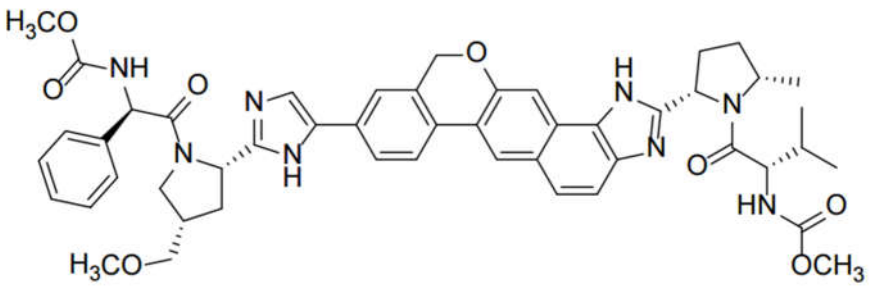
Velpatasvir PK Fact Sheet

Details

Generic Name	Velpatasvir
Trade Name	Epclusa® (co-formulated with sofosbuvir) Vosevi® (co-formulated with sofosbuvir and velpatasvir)
Class	HCV NS5A inhibitor
Molecular Weight	883
Structure	

Summary of Key Pharmacokinetic Parameters

Velpatasvir is available in a fixed-dose combination product with sofosbuvir or with sofosbuvir and voxilaprevir.

Linearity/non-linearity	Velpatasvir AUC increases in a greater than proportional manner from 5 mg to 50 mg and in a less than proportional manner from 50 mg to 450 mg in healthy volunteers. However, velpatasvir exhibited more than or near dose-proportional increase in exposures from 25 mg to 150 mg in HCV-infected patients.
Steady state	Achieved after approximately 3-4 days of once daily dosing.
Plasma half life	~15 h
Cmax	259 (54.3) ng/ml (mean, %CV, based on population PK modelling)
Ctrough	42 (67.3) ng/ml (mean, %CV, based on population PK modelling)
AUC	2980 (51.3) ng.h/ml (mean, %CV, based on population PK modelling)
Bioavailability	Not determined
Absorption	Relative to fasting conditions, administration of a single dose of Epclusa with a moderate fat (~600 kcal, 30% fat) or high fat (~800 kcal, 50% fat) meal increased velpatasvir AUC by 34% and 21% and increased Cmax by 31% and 5%, respectively. Velpatasvir, administered as Epclusa, can be taken with or without food.
Protein Binding	>99.5%
Volume of Distribution	Not determined
CSF:Plasma ratio	Not determined
Semen:Plasma ratio	Not determined
Renal Clearance	0.4%
Renal Impairment	No dose adjustment of Epclusa is required for patients with mild or moderate renal impairment. The safety and efficacy of Epclusa has not been assessed in patients with severe renal impairment (estimated glomerular filtration rate [eGFR] <30 mL/min/1.73 m^2) or end stage renal disease (ESRD) requiring haemodialysis. No dosage recommendation can be given for patients with severe renal impairment or ESRD.
Hepatic Impairment	No dose adjustment of Epclusa is required for patients with mild, moderate, or severe hepatic impairment (CPT Class A, B, or C). Safety and efficacy of Epclusa have been assessed in patients with CPT Class B cirrhosis, but not in patients with CPT Class C cirrhosis.

Metabolism and Distribution

Metabolised by	CYP2B6, CYP2C8, CYP3A4
Inducer of	Does not induce metabolising enzymes or transporters via the AhR or PXR receptors [1] (e.g. CYPs 1A1, 1A2, 1B1, 2A6, 2B6, 2C9, 3A4; UGT1A1; BRCP, MDR1; MRP2, OATP2)
Inhibitor of	Inhibits P-gp (weak), BCRP (moderate), OATP1B1 (weak), OATP1B3 (weak) [1]. At clinically relevant plasma concentrations, velpatasvir is not an inhibitor of BSEP, NTCP, OATP1A2, OCT1, OCT2, OAT1, OAT3, MRP2, MATE1 transporters or CYP or UGT1A1 enzymes.
Transported by	P-gp, BCRP, OATP1B1, OATP1B3.

References

Unless otherwise stated (see below), information is from:
Epclusa® Summary of Product Characteristics, Gilead Sciences Ltd.
Epclusa® US Prescribing Information, Gilead Sciences Inc.
Vosevi® Summary of Product Characteristics, Gilead Sciences Ltd.
Vosevi® US Prescribing Information, Gilead Sciences Inc.

1. Mogalian E, German P, Kearney BP, *et al*. 2016, *Clin Pharmacokinet*, 55: 605-613.