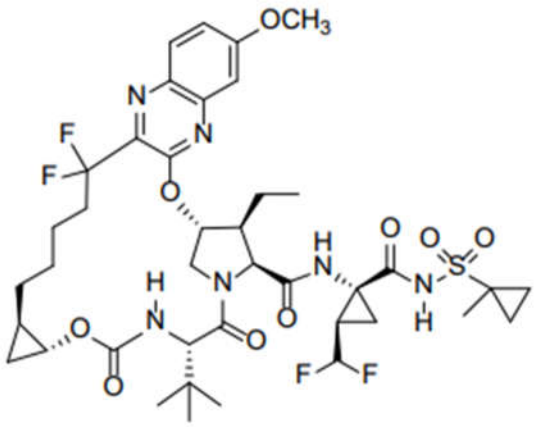
Voxilaprevir PK Fact Sheet

Details

Generic Name	Voxilaprevir
Trade Name	Vosevi® (co-formulated with sofosbuvir and velpatasvir)
Class	HCV NS3/4A inhibitor
Molecular Weight	868.9
Structure	

Summary of Key Pharmacokinetic Parameters

Voxilaprevir is available in a fixed-dose combination product with sofosbuvir and velpatasvir.

Linearity/non-linearity	Voxilaprevir AUC (studied under fed conditions) increases in a greater than dose-proportional manner over the dose range of 100 to 900 mg.
Steady state	Achieved after approximately 7 days of once daily dosing [1]
Plasma half life	~33h
Cmax	192 (85.8) ng/ml (mean, %CV, based on population PK modelling)
Ctrough	47 (82.0) ng/ml (mean, %CV, based on population PK modelling)
AUC	2577 (73.7) ng.h/ml (mean, %CV, based on population PK modelling)
Bioavailability	Not determined
Absorption	Relative to fasting conditions, administration of voxilaprevir with food increased voxilaprevir AUC and Cmax by 112-435% and 147-680%, respectively. Vosevi should be taken with food.
Protein Binding	>99%
Volume of Distribution	Not reported
CSF:Plasma ratio	Not reported
Semen:Plasma ratio	Not reported
Renal Clearance	Not excreted in urine
Renal Impairment	No dose adjustment is required for patients with mild or moderate renal impairment. The safety and efficacy have not been assessed in patients with severe renal impairment or end-stage renal disease requiring haemodialysis
Hepatic Impairment	No dose adjustment is required for patients with mild hepatic impairment (Child-Pugh A). Voxilaprevir is not recommended in patients with moderate or severe hepatic impairment (Child-Pugh B or C)

Metabolism and Distribution

Metabolised by	CYP3A4, CYP1A2, CYP2C8
Inducer of	None expected. 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, BCRP, OATP1B1, OATP1B3 At clinically relevant concentrations, voxilaprevir is not an inhibitor of hepatic transporters OCT1, renal transporters OCT2, OAT1, OAT3 or MATE1, or CYP or UGT1A1 enzymes.
Transported by	P-gp, BCRP, OATP1B1, OATP1B3.

References

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

1. Clinical Pharmacology Review for NDA 209195, FDA Center for Drug Evaluation and Research, May 2017. Available at https://www.accessdata.fda.gov/drugsatfda_docs/nda/2017/209195Orig1s000ClinPharmR.pdf