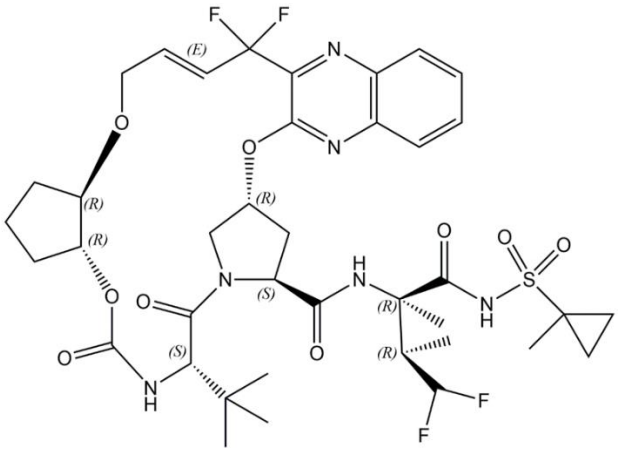
Glecaprevir PK Fact Sheet

Details

Generic Name	Glecaprevir
Trade Name	Maviret®, Mavyret®, (co-formulated with pibrentasvir)
Class	HCV NS3/4A inhibitor
Molecular Weight	838.87
Structure	

• X H_2O

Summary of Key Pharmacokinetic Parameters

Glecaprevir is available in a fixed-dose combination product with pibrentasvir.

Linearity/non-linearity	Glecaprevir AUC increases in a greater than dose-proportional manner (1200 mg once daily had 516-fold higher exposure than 200 mg once daily) which may be related to saturation of uptake and efflux transporters
Steady state	Achieved after 7 days of once daily dosing [1]
Plasma half-life	6-9 h
Cmax	597 (114) ng/mL (geometric mean, %CV), in non-cirrhotic HCV-infected subjects
C24	3.07 (54), 5.50 (46), 3.72 (71) ng/mL (geometric mean, %CV), in healthy White, Han Chinese and Japanese adults, respectively [2]
AUC	4800 (122) ng·h/mL (geometric mean, %CV), in non-cirrhotic HCV-infected subjects
Bioavailability	Not reported
Absorption	Compared to fasting, a moderate to high-fat meal increased glecaprevir exposure by 83-163%.
Protein Binding	97.5%
Volume of Distribution	Not reported
CSF:Plasma ratio	Not reported
Semen:Plasma ratio	Not reported
Renal Clearance	0.7% of dose excreted in urine
Renal Impairment	No dosage adjustment is required in patients with mild, moderate or severe renal impairment, including those on dialysis.
Hepatic Impairment	No dose adjustment is required in patients with mild hepatic impairment (Child-Pugh A). Glecaprevir is not recommended in patients with moderate hepatic impairment (Child-Pugh B) and is contraindicated in patients with severe hepatic impairment (Child-Pugh C).

Metabolism and Distribution

Metabolised by	CYP3A (minimal) – glecaprevir is mainly eliminated by biliary/faecal excretion
Inducer of	None expected
Inhibitor of	Inhibitor of P-gp, BCRP, OATP1B1, OATP1B3, BSEP. Weak inhibitor of CYP3A, CYP1A2, UGT1A1 (significant interactions are not expected with substrates of these enzymes). Significant inhibition of CYP2C9, CYP2C19, CYP2D6, UGT1A6, UGT1A9, UGT1A4, UGT2B7, OCT1, OCT2, OAT1, OAT3, MATE1 or MATE2K are not expected.
Transported by	P-gp, BCRP, OATP1B1, OATP1B3

References

Unless otherwise stated (see below), information is from:
Maviret Summary of Product Characteristics, AbbVie Ltd.
Mavyret Prescribing Information, AbbVie Inc.

1. Pharmacokinetic interactions and safety of coadministration of glecaprevir and pibrentasvir in healthy volunteers. Lin C, Dutta S, Zhao W et al. *Eur J Drug Metab Pharmacokinet*, 2018, 43(1): 81-90.
2. Pharmacokinetics, safety, and tolerability of glecaprevir and pibrentasvir in healthy White, Chinese, and Japanese adult subjects. Lin C, Dutta S, Ding B, et al. *J Clin Pharmacol*, 2017, 57(12): 1616-1624.