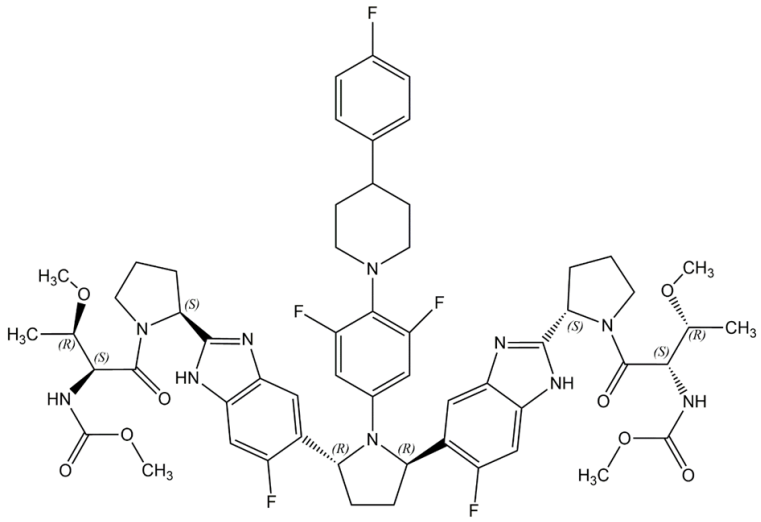
Pibrentasvir PK Fact Sheet

Details

Generic Name	Pibrentasvir
Trade Name	Maviret®, Mavyret®, (co-formulated with glecaprevir)
Class	HCV NS5A inhibitor
Molecular Weight	1113.18
Structure	

Summary of Key Pharmacokinetic Parameters

Pibrentasvir is available in a fixed-dose combination product with glecaprevir.

Linearity/non-linearity	Pibrentasvir AUC increased in a greater than dose-proportional manner at doses up to 120 mg, (over 10-fold exposure increase at 120 mg compared to 30 mg), but exhibited linear pharmacokinetics at doses ≥120 mg. The non-linear exposure increase below 120 mg may be related to saturation of efflux transporters.
Steady state	Achieved after 5 days of once daily dosing [1]
Plasma half-life	23-29 h in healthy subjects; 13 h in non-cirrhotic HCV-infected subjects
Cmax	110 (49) ng/mL (geometric mean, %CV), in non-cirrhotic HCV-infected subjects
C24	9.94 (75), 5.33 (48), 6.68 (60) ng/mL (geometric mean, %CV), in healthy White, Han Chinese and Japanese adults, respectively [2]
AUC	1430 (57) ng·h/mL (geometric mean, %CV), in non-cirrhotic HCV-infected subjects
Bioavailability	Pibrentasvir bioavailability increases 3-fold when given with glecaprevir than when given alone.
Absorption	Compared to fasting, a moderate to high-fat meal increased pibrentasvir exposure by 40-53%.
Protein Binding	>99.9%
Volume of Distribution	Not determined
CSF:Plasma ratio	Not determined
Semen:Plasma ratio	Not determined
Renal Clearance	No renal clearance
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). Pibrentasvir 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	Not metabolised - pibrentasvir is 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

References

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

1. Pharmacokinetics, safety, and tolerability following single and multiple doses of pibrentasvir in a first-in-human study. Lin C, Dutta S, Asatryan A, et al. *Clin Pharmacol Drug Dev*, 2018, 7(1): 44-52.
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.