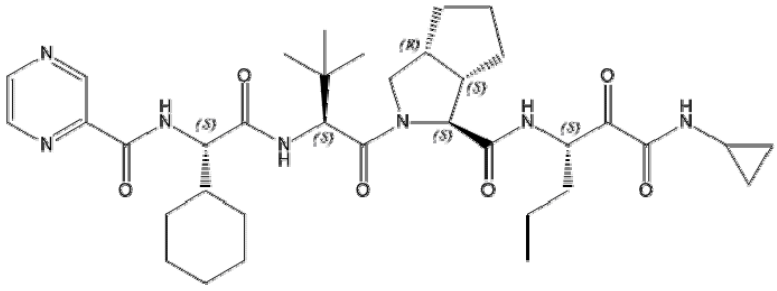
Telaprevir PK Fact Sheet

Details

Generic Name	Telaprevir
Trade Name	Incivek®. Incivo®
Class	HCV NS3/4A protease inhibitor
Molecular Weight	679.85
Structure	

Summary of Key Pharmacokinetic Parameters

Linearity/non-linearity	After multiple doses, an increase in dose from 750 mg every 8 h to 1875 mg every 8 h resulted in less than proportional increases (~40%) in telaprevir exposure.
Steady state	No data
Plasma half life	9-11 h
Cmax	3510 ± 1280 ng/ml (mean ± sd, 750 mg every 8 h, steady state)
Cmin	2030 ± 930 ng/ml (mean ± sd, 750 mg every 8 h, steady state)
AUC	22300 ± 8650 ng.h/ml (mean ± sd, 750 mg every 8 h, steady state) Telaprevir total exposure (AUC24h,ss) was similar regardless of whether the total daily dose of 2250 mg was administered as 750 mg every 8 hours or 1125 mg twice daily.
Bioavailability	Formal bioavailability not determined.
Absorption	Telaprevir AUC was increased by 237% when administered with a standard fat meal (containing 533 kcal and 21 g fat) compared to when administered under fasting conditions. In addition, the type of meal significantly affects exposure to telaprevir. Relative to fasting, when telaprevir was administered with a low-fat meal (249 kcal, 3.6 g fat) and a high-fat meal (928 kcal, 56 g fat), telaprevir AUC was increased by approximately 117% and 330%, respectively. Doses of telaprevir were administered within 30 minutes of completing a meal or snack containing approximately 20 grams of fat in the Phase 3 trials. Therefore, telaprevir should always be taken with food (not low fat).
Protein Binding	59-76%
Volume of Distribution	~252 L
CSF:Plasma ratio	Not studied
Semen:Plasma ratio	Not studied
Renal Clearance	~1% of total ^{14}C-telaprevir recovered in urine.

Renal Impairment	No dose adjustment is necessary for telaprevir in HCV-infected patients with mild, moderate or severe renal impairment. Telaprevir has not been studied in HCV-infected patients with CrCl ≤50 mL/min, in patients with end-stage renal disease (ESRD) or in patients on haemodialysis. After administration of a single dose of 750 mg to HCV-negative subjects with severe renal impairment (CrCl <30 mL/min), the LS means of telaprevir Cmax and AUC were increased by 3% and 21%, respectively, compared to healthy subjects.
Hepatic Impairment	No dose adjustment of telaprevir is necessary for patients with mild hepatic impairment (Child-Pugh A, score 5-6). Steady-state exposure to telaprevir was reduced by 15% in HCV-negative subjects with mild hepatic impairment (Child-Pugh Class A) compared to healthy subjects. Telaprevir is not recommended for patients with moderate or severe hepatic impairment (Child-Pugh B or C, score greater than or equal to 7) or patients with decompensated liver disease. Steady-state exposure to telaprevir was reduced by 46% in HCV-negative subjects with moderate hepatic impairment (Child-Pugh Class B) compared to healthy subjects. The appropriate dose of telaprevir in HCV-infected subjects with moderate or severe hepatic impairment has not been determined.

Metabolism and Distribution

Metabolised by	CYP3A
Inducer of	Low potential to induce CYP2C, CYP3A and CYP1A in vitro. Does not induce CYP1A, CYP3A, CYP2B6 or CYP2C in vitro.
Inhibitor of	CYP3A, P-gp, OATP1B1, OATP1B2. Potential inhibitor of UGT1A3, but clinical relevance unknown. Does not inhibit CYP1A2, CYP1A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, UGT1A9 or UGT2B7 in vitro. Does not inhibit the transporters BCRP, MRP2, OCT2 or OAT1 in vitro.
Transported by	P-gp

References

Unless otherwise stated (see below), information is from:
Incivo European Summary of Product Characteristics, Janssen-Cilag Ltd.
Incivek® US Prescribing Information, Vertex Pharmaceuticals Inc.