Doravirine PK Fact Sheet

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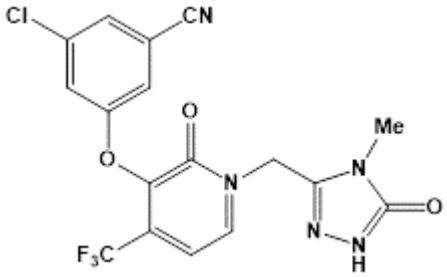
Details

Generic Name	Doravirine
Trade Name	Pifeltro® Delstrigo® (with lamivudine and tenofovir disoproxil fumarate)
Class	Non-nucleoside reverse transcriptase inhibitor (NNRTI)
Molecular Weight	425.75
Structure	

Summary of Key Pharmacokinetic Parameters

Linearity/non-linearity	AUC, Cmax and C24 increased in a slightly less that dose proportional manner over a dose range of 6-1200 mg.[1]
Steady state	~2 days
Plasma half life	~15 h
Cmax	0.962 (19) µg/mL (100 mg once daily to HIV-1+ subjects, geometric mean (%CV))
C24	0.396 (63) µg/mL (100 mg once daily to HIV-1+ subjects, geometric mean (%CV))
AUC	16.1 (29) µ.h/mL (100 mg once daily to HIV-1+ subjects, geometric mean (%CV))
Bioavailability	64%
Absorption	AUC, Cmax, and C24 increased by 16%, 3%, and 36%, respectively, when given with food. Doravirine can be taken with or without food.
Protein Binding	76%
Volume of Distribution	60.5 L
CSF:Plasma ratio	Undetermined
Semen:Plasma ratio	Undetermined
Renal Clearance	The major route of elimination is metabolism, with 6% eliminated unchanged in the urine. Renal clearance is 9.3 mL/min.
Renal Impairment	Single dose exposure of doravirine was 43% higher in subjects with severe renal impairment (n=8) than in subjects without renal impairment (n=8). No dosage adjustment is required in patients with mild, moderate, or severe renal impairment. In a population pharmacokinetic analysis, renal function did not have a clinically relevant effect on doravirine pharmacokinetics. Doravirine has not been studied in patients with end-stage renal disease or in patients undergoing dialysis.
Hepatic Impairment	No clinically significant difference in the pharmacokinetics of doravirine was observed in subjects with moderate hepatic impairment (Child-Pugh score B) compared to subjects without hepatic impairment. No dosage adjustment is required in patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. Doravirine has not been studied in subjects with severe hepatic impairment (Child-Pugh score C)

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Metabolism and Distribution

Metabolised by	CYP3A4 (major), CYP3A5 (minor).[2]
Inducer of	Minimal potential to induce CYP3A4.[1]
Inhibitor of	Doravirine did not inhibit major drug metabolizing enzymes in vitro, including CYPs 1A2, 2B6, 2C8, 2C9, 2C19, 2D6, 3A4, and UGT1A1 and is not likely to be an inducer of CYPs 1A2, 2B6, or 3A4. Based on in vitro assays, doravirine is not likely to be an inhibitor of OATP1B1, OATP1B3, P-gp, BSEP, OAT1, OAT3, OCT2, MATE1, and MATE2K.
Transported by	P-gp, but does not have a significant role doravirine absorption or elimination.[1] Not transported by OATP1B1.[1]

References

Unless otherwise stated (see below), information is from:

Pifeltro Summary of Product Characteristics, Merck Sharp & Dohme Ltd,
Pifeltro US Prescribing Information, Merck & Co Inc.

1. Anderson MS, Gilmartin J, Cilissen C, *et al.* Safety, tolerability and pharmacokinetics of doravirine, a novel HIV non-nucleoside reverse transcriptase inhibitor, after single and multiple doses in healthy subjects. *Antivir Ther*. 2015, 20(4): 397-405.

2. Sanchez RI, Fillgrove KL, Yee KL, *et al*. Characterisation of the absorption, distribution, metabolism, excretion and mass balance of doravirine, a non-nucleoside reverse transcriptase inhibitor in humans. *Xenobiotica*, 2019, 49(4):422-432.

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