

# Population Pharmacokinetic Analysis of Doravirine in Real-World People with HIV

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October 20, 2023

## Abstract

**Aim:** The pharmacokinetics of doravirine have been studied in clinical trials, but not in real-world settings. Our study aims to characterize and identify factors influencing doravirine pharmacokinetics (a CYP3A4 substrate) in real-world people with HIV (PWH). **Methods:** A total of 174 doravirine concentrations measured in 146 PWH followed up in the therapeutic drug monitoring (TDM) program at the University Hospital of Lausanne (Switzerland) between 2019 and 2023 were included in the analysis. Population pharmacokinetic analysis and Monte Carlo simulations to investigate the clinical significance of the covariates retained in the final model were performed using NONMEM. **Results:** A one-compartment model with first-order absorption and linear elimination best described doravirine pharmacokinetics. Potent CYP3A4 inhibitors and, to a lesser extent age, were the only tested covariates to significantly impact doravirine clearance (CL). Potent CYP3A4 reduced CL by 50%, and a 30% decrease in CL was observed in an 80-year-old compared to a 55-year-old PWH. The effect of potent CYP3A4 inhibitors was prominent, explaining 59% of between-subject variability in CL. Model-based simulations predicted 2.8-fold and 1.6-fold increases in median steady-state trough and maximum doravirine concentrations, respectively, when a potent CYP3A4 inhibitor was co-administered. **Conclusion:** Our findings show that potent CYP3A4 inhibitors and age influence doravirine pharmacokinetics. However, given the good tolerability of doravirine, dosing adjustment of doravirine is probably not mandatory in those situations. TDM remains useful essentially in specific clinical situations, such as hepatic impairment, suspected non-adherence or pregnancy.

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