# Absolute Bioavailability of Edoxaban in Healthy Subjects

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Purpose: Edoxaban is a selective, oral direct factor Xa inhibitor currently in phase 3 clinical development for stroke prevention in AF and the treatment and secondary prevention of VTE. The objectives of this study were to assess the absolute bioavailability and disposition of edoxaban (PO vs IV) in healthy subjects.

Methods: Thirty-five healthy adult volunteers were randomized to edoxaban 60 mg PO (2 x 30 mg tablets) or 30 mg IV solution infused over 30 minutes using a Baxter Flo-Gard infusion pump. Blood and urine samples for pharmacokinetic assessment were collected up to 72 hours post-dose and the plasma and urine concentrations of edoxaban and its metabolite, M-4, were determined by validated HPLC-MS/MS methods. Absolute bioavailability (F) was calculated as log-transformed dose-adjusted $AUC_{0\text{-}inf}$ for edoxaban obtained from PO and IV treatments [$F=(AUC_{PO}/Dose_{PO}) / (AUC_{IV}/Dose_{IV})$].

Results: The pharmacokinetic parameters of edoxaban for both treatments are presented below. The ratios of geometric LSM of the dose-adjusted $AUC_{0\text{-}inf}$ between PO and IV indicated F=61.80% (95% CI: 57.70, 66.19). Both treatments were well tolerated and primary AEs were mild.

Pharmacokinetic Parameters for Edoxaban

| Parameter,<br>Arithmetic Mean (± SD) | 60 mg PO<br>N=35 | 30 mg IV<br>N=35 |
|---|---|---|
| $AUC_{0\text{-}inf}$ (ng•h/mL) | 1766 ± 435.3 | 1317 ± 189.4 |
| $C_{max}$ (ng/mL) | 256 ± 87.7 | 424 ± 114.8 |
| $T_{max}$ (h)[a] | 1.02 (0.500-3.00) | 0.483 (0.250-1.98) |
| $t_{½}$ (h) | 11.5 ± 5.63 | 6.70 ± 2.547 |
| $V_{ss}$ (L) | NA | 107 ± 19.9 |
| CL/F (L/h) | 35.7 ± 7.63 | NA |
| CL (L/h) | NA | 21.8 ± 3.03 |
| $CL_R$ (L/h) | 9.95 ± 2.32 | 10.7 ± 3.00 |
| Fe (%) | 28.6 ± 6.85 | 48.6 ± 9.66 |
| F (%)[b] | 61.80 (57.70-66.19) | |

NA = not calculated.

[a] Median (min-max).

[b] Ratio of geometric LSM of the dose-adjusted values.

Conclusion: The absolute bioavailability of edoxaban following a single 60 mg PO dose was 61.80%.