

Parameter estimates and precision of original model [1]

PK parameter	Estimates	RSE, %
CL_{20}/F [L/h]	9.34	6.20
V_2/F [L]	753	9.00
k_{12} [1/h]	1.90	20.2
CL_{23}/F [L/h]	0.324	17.0
Q/F [L/h]	61.8	65.4
t_{lag} [h]	0.455	10.4
θ_{CYP2D6}	0.262	14.0
$\theta_{CYP3A4/5}$	0.157	72.0
ω CL_{20}/F , %CV	37.8	19.2
ω V_2/F , %CV	26.6	53.9
ω CL_{23}/F , %CV	25.5	19.3
ρ (ω CL_{20} - V_2/F), %	61.3	31.2
σ_{TAM} , %CV	13.8	11.3
σ_{ENDX} , %CV	18.9	10.1
ρ (σ_{TAM} - $ENDX$), %	62.2	22.6

CL_{20}/F , relative clearance of tamoxifen; CL_{23}/F : Clearance from metabolism compartment i.e. endoxifen formation; CV , coefficient of variation; $ENDX$, endoxifen; k_{12} ,absorption rate constant; Q/F , liver flow; RSE , relative standard error; TAM , tamoxifen; t_{lag} , lag time; V_2/F , relative volume of distribution; $\theta_{CYP3A4/5}$, CYP3A4/5 covariate effect; θ_{CYP2D6} , CYP2D6 covariate effect; ρ , correlation coefficient; σ , residual unexplained variability; ω , inter-individual variability; $st-st$, steady-state assumed at specific day;

[1] Ter Heine R, Binkhorst L, de Graan AJM, et al. Population pharmacokinetic modelling to assess the impact of CYP2D6 and CYP3A metabolic phenotypes on the pharmacokinetics of tamoxifen and endoxifen. Br. J. Clin. Pharmacol. 2014;78:572–86.