Table S4 Parameters used in the cimetidine PBPK model

Parameter (unit)	Value	Reference
Physicochemical		
pKa	6.9	1
logP	0.48	1
Absorption-related		
k_a (/h)	0.70	1
T_{lag} (h)	0.15	1
FaFg	0.92	1
Distribution-related		
$f_{u,cim}$	0.80	1
R_b	0.97	1
$K_{p,adipose}$	0.24	1
$K_{p,muscle}$	0.86	1
$K_{p,skin}$	0.72	1
Liver-related		
PS_{act} (L/h)	12.0	2
R_{dif}	1.16	2
CL_{met}(L/h)	11.3	1
Kidney-related		
Pd (m/h)	$7.9*10^{-5}$	3
λ	0.1	4
$K_{m,OCT2}$ (μM)	72.6	1
$V_{max,OCT2}$ (μmol/h)*	7265	1
$R_{OCT2,inf/eff}$	1.32	5
$K_{m,OAT3}$ (μM)	161	1
$V_{max,OAT3}$ (μmol/h)*	4124	1
$K_{m,MATE}$ (μM)	7.7	1
$V_{max,MATE}$ (μmol/h)*	453	1

k_a, absorption rate constant; T_{lag}, intestinal absorption lag time; FaFg, intestinal availability; $f_{u,cim}$, unbound fraction in plasma; $K_{p,adipose}$, adipose/blood concentration ratio; $K_{p,muscle}$, muscle/blood centration ratio; $K_{p,skin}$, skin/blood concentration ratio; P_d, permeability value; λ, the ratio of passive diffusion for an ionized form to that for an unionized form;PS_{OCT2}, clearance by OCT2; $R_{OCT2,inf/eff}$, OCT2-mediated influx-to-efflux clearance ratio; PS_{OAT3}, clearance by OAT3; PS_{MATE}, clearance by MATEs; PS_{act}, hepatic active clearance; R_{dif},

passive-to-active clearance ratio; CL_{met}, hepatic metabolic clearance;

**: Value were calculated from Burt et al., 2016 including RAF.*

Refence for Supplemental Table 4

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