**Supplement table 1: Physicochemical properties and pharmacokinetic parameters of chloroquine used for the development of the PBPK model**

|  |  |
| --- | --- |
| Parameter | Input Value |
| Physicochemical properties |  |
| Molecular weight (g/mol) | 319.87 |
| Log *P* | 4.37 |
| Compound type | Diprotic base |
| pKa  | 9.94, 8.40 |
| Blood-to-plasma partition ratio | 3.50 |
| Hematocrit | 45.0 |
| Fraction unbound in plasma | 0.40 |
| Absorption |  |
| Absorption model | First-order  |
| Absorption rate constant (h-1) | 0.50 |
|  Polar surface area (Å2) | 25.7 |
|  Number of hydrogen bond donors | 1 |
| Distribution |  |
|  Distribution model | Full PBPK model |
|  User-defined additional Organ | Perfusion limited |
|  Vss (L/kg) | Predicted\* |
|  Kp scalar | 2.66 |
| Elimination |  |
|  Clearance type | Enzyme kinetics |
|  CLint of recombinant CYP2C8 (µL/min/ pmol of isoform) | 0.269 |
|  CLint of recombinant CYP3A4 (µL/min/ pmol of isoform) | 0.0283 |
|  Additional clearance of HLM (µL/min/ mg protein) | 2.58 |
|  Typical renal clearance (L/h) | 20.8 |

 \*Rodgers and Rowland prediction method was used.

Abbreviations: *P*, octanol-water partition coefficient; PBPK, physiologically-based pharmacokinetic; Vss, volume of distribution at steady-state; Kp, partition coefficient; HLM, human liver microsome.

**Supplement table 2: Physicochemical properties and pharmacokinetic parameters of hydroxychloroquine used for the development of the PBPK model**

|  |  |
| --- | --- |
| Parameter | Input Value |
| Physicochemical properties |  |
| Molecular weight (g/mol) | 335.87 |
| Log *P* | 3.84 |
| Compound type | Diprotic base |
| pKa  | 9.67, 8.27 |
| Blood-to-plasma partition ratio | 7.20 |
| Hematocrit | 45.0 |
| Fraction unbound in plasma | 0.50 |
| Absorption |  |
| Absorption model | First-order |
| Absorption rate constant (h-1) | 0.80 |
| Lag time (h) | 0.43 |
|  Polar surface area (Å2) | 25.7 |
|  Number of hydrogen bond donors | 2 |
| Distribution |  |
|  Distribution model | Full PBPK model |
|  User-defined additional Organ | Perfusion limited |
|  Vss (L/kg) | Predicted\* |
|  Kp scalar | 2.45 |
| Elimination |  |
|  Clearance type | Enzyme kinetics |
|  Additional clearance of HLM (µL/min/ mg protein) | 14.0 |
|  Typical renal clearance (L/h) | 12.7 |

 \*Rodgers and Rowland prediction method was used.

Abbreviations: *P*, octanol-water partition coefficient; PBPK, physiologically-based pharmacokinetic; Vss, volume of distribution at steady-state; Kp, partition coefficient; HLM, human liver microsome.