

PHAR:8230 (46:170)
Clinical Pharmacokinetics Equations

Adults: (≥ 17 years)

$$CrCl \text{ (ml/min)} = \frac{(140 - \text{Age}) \cdot CrCl/Wt}{72 \cdot SrCr} \cdot (0.85 + Sex \cdot 0.15)$$

If the patient is $<$ IBW, use $Wt = ABW$.

If the patient is $>$ IBW and $BMI < 25 \text{ Kg/m}^2$, $Wt = IBW$

If the patient has a $BMI \geq 25 \text{ Kg/m}^2$, $Wt = AdjWT$

$$CorrSrCr = (SrCr + 0.07) / 0.987$$

Neonates: (< 2 months)

$$CrCl \text{ (ml/min/1.73m}^2) = \frac{0.45 \cdot (CmHt.)}{SrCr}$$

Pediatrics: (2 months – 16 years)

$$CrCl \text{ (ml/min/1.73m}^2) = \frac{3.5 \cdot \text{Age} + 23.6}{SrCr}$$

IBW (males)

$$50 \text{ Kg} + 2.3 \text{ Kg/inch over 5 feet}$$

IBW (females)

$$45.5 \text{ Kg} + 2.3 \text{ Kg/inch over 5 feet}$$

$$BMI = Wt \text{ (Kg)} / (Ht \text{ (In)} \cdot 0.0254)^2$$

If ActBW is $> 30\%$ over IBW, then

$$DWT = IBW + 0.4 \cdot (\text{ActBW} - IBW)$$

If $BMI \geq 25 \text{ Kg/m}^2$, then

$$CrCl - WT = IBW + 0.4 \cdot (\text{ActBW} - IBW)$$

$$BSA = Wt^{0.5378} \cdot Ht^{0.3964} \cdot 0.024265$$

$$CrCl \text{ Norm} = CrCl \cdot 1.73 / BSA$$

$$GFR = 175 \cdot SrCr^{-1.154} \cdot Age^{-0.203} \cdot (0.742 + Sex \cdot 0.258) \cdot (1 + 0.21 \cdot Black) \quad \begin{array}{l} \text{Black} = 1, \text{ else} = 0, \\ \text{Sex: Male} = 1, \text{ female} = 0 \end{array}$$

$$GFR \text{ (CKD - EPI)} = (144 - (Sex \cdot 3)) \cdot (1 + 0.155 \cdot Black) \cdot 0.993^{Age} \cdot \left(\frac{SrCr}{(0.7 + (0.2 \cdot Sex))} \right)^{-0.329 - SrCrExp}$$

[where Sex = 1 for male, 0 for female, Black = 1 for Black, 0 for other races. and
If $SrCr > (0.7 + 0.2 \cdot Sex)$ Then $SrCrExp = 0.88$, Else $SrCrExp = Sex \cdot 0.082$]

Population Estimates

Volume of distribution (V)

Aminoglycosides:

$$V_{ss} \text{ (L)} = 0.225 \text{ L/kg} \times DWT$$

$$V_{ss} \text{ (dehydrated)} = 0.15 \text{ L/kg} \times DWT$$

$$V_{ss} \text{ (Fluid overload)} = 0.30 \text{ L/kg} \times DWT$$

Vancomycin:

$$V_{ss} \text{ (L)} = 0.7 \text{ L/Kg} \times \text{ActWT}$$

Elimination rate constant (k)

Gentamicin

$$K_e = 0.015 + (0.00285 \times CrCl)$$

Tobramycin

$$K_e = 0.010 + (0.0031 \times CrCl)$$

Amikacin

$$K_e = 0.010 + (0.0024 \times CrCl)$$

Vancomycin

$$K_e = [44 + (8.3 \times CrCl)] / 10000$$

1. Calculate the elimination rate constant.

$$k_e = \frac{\ln C_1 - \ln C_2}{t_2 - t_1} = \frac{\ln C_{pk} - \ln C_{tr}}{t_{tr} - t_{pk}} = \frac{\ln(C_{pk} / C_{tr})}{\tau - t_{inf} - t_{pi}}$$

2. Calculate C_0 (t_{pk} = elapsed time from start of infusion)

$$C_0 = \frac{C_{pk}}{e^{-k_e(t_{pk} - t_{inf})}}$$

3. Calculate the half-life.

$$t_{1/2} = \frac{\ln 2}{k_e}$$

4. Calculate the volume of distribution.

$$V_{ss} = \frac{R_0}{k_e} \cdot \frac{1 - e^{-k_e t_{inf}}}{(C_0 - C_{tr} \cdot e^{-k_e t_{inf}})}$$

5. Calculate the dosing interval.

$$\tau = \frac{\ln(C_{Max,desired} / C_{Min,desired})}{k_e} + t_{inf}$$

6. Calculate the new infusion rate.

$$R_0 = C_{Max,desired} \cdot k_e \cdot V_{ss} \cdot \frac{(1 - e^{-k_e \tau})}{(1 - e^{-k_e t_{inf}})}$$

7. Calculate the new peak.

$$C_{ss,pk} = \frac{R_0}{V_{ss} \cdot k_e} \cdot \frac{(1 - e^{-k_e t_{inf}})}{(1 - e^{-k_e \tau})}$$

8. Calculate the new trough.

$$C_{ss,tr} = C_{ss,pk} \cdot e^{-k_e(\tau - t_{inf})}$$

TR Only: $(Dose/\tau)_{new} = (Dose/\tau)_{current} * C_{desired}/C_{measured}$ [C_{desired} = Target 15 mg/L]

Target Drug Concentrations

	Trough	Peak (Life Threatening infection)	Peak (Serious Infection)	Peak (Synergy/UTI)	Infusion Time
Gentamicin	< 2 mg/L	8 to 10 mg/L	6 to 8 mg/L	4 to 6 mg/L	0.5 Hr.
Tobramycin	< 2 mg/L	8 to 10 mg/L	6 to 8 mg/L	4 to 6 mg/L	0.5 Hr.
Amikacin	< 10 mg/L	25 to 30 mg/L	20 to 25 mg/L	15 to 20 mg/L	0.5 Hr.
Vancomycin	10-20 mg/L		30 to 40 mg/L		1.5 Hr. (≤ 1.25 g) 2 Hr. (1.5 – 2 g)

Extended-Interval Dosing

Initial Dosing Regimen - Adults:

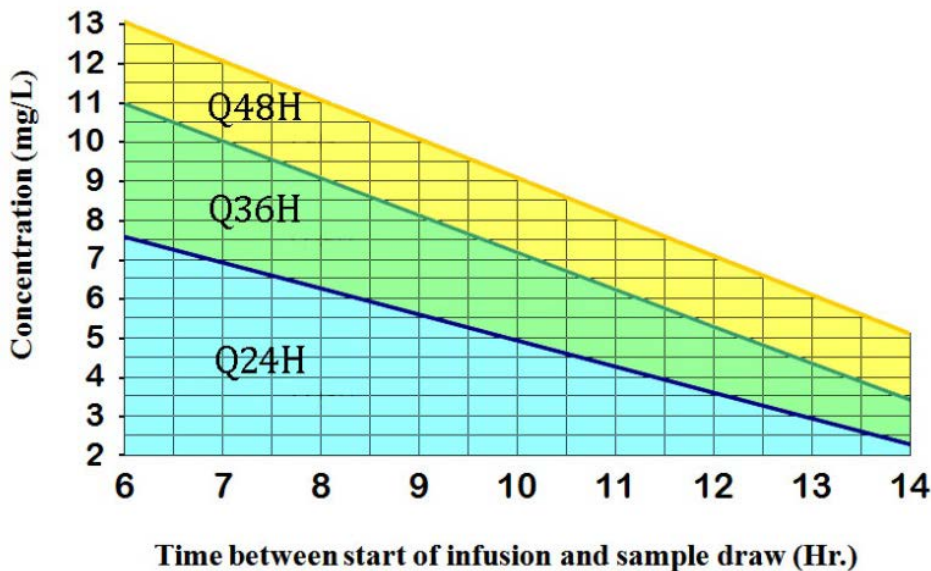
<u>Creatinine Clearance</u>	<u>Dose and Dosing Interval</u>
≥ 60 ml/min	7 mg/kg every 24 hours
40 to 59 ml/min	7 mg/kg every 36 hours
20-39 ml/min	7 mg/kg every 48 hours
< 20 ml/min	Use conventional dosing approach.

Dosing is based on ABW, unless the patient is >30% IBW, use DWT

Initial Dosing Regimen - Children:

<u>Age</u>	<u>Dose and Dosing Interval</u>
3 months – 2 years	9.5 mg/kg every 24 hours
2 – 8 years	8.5 mg/kg every 24 hours
> 8 Years	7.0 mg/kg every 24 hours

Hartford Hospital Nomogram



Monitoring: Obtain a single serum level 6 to 14 hours after the start of infusion following the administration of the first dose. Evaluate according to the nomogram below. If the patient is on a transition line, choose the longer interval. If the level is off the nomogram, hold the next dose and obtain serial levels to calculate drug clearance according to conventional dosing equations.

Patient Exclusion: Extended-interval dosing is not recommended in pediatrics, pregnancy, burn patients (>20%), ascites, dialysis, enterococcal endocarditis, and patients with an estimated creatinine clearance of < 20 ml/min.

Hartford nomogram for gentamicin and tobramycin at 7 mg/kg