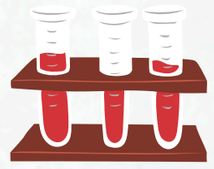
TDM SAMPLING GUIDELINE



DRUG	TIME TO REACH STEADY STATE		THERAPEUTIC RANGE (mg/L)	THERAPEUTIC RANGE (µmol/L)	CONVERSION FACTORS mg/L to µmol/L (x) µmol/L to mg/L (÷)
Available TDM test in HSB					
Gentamicin	**SDD:** After 24 hours (Sample at least after 2 doses) **Conventional:** after 3rd dose	**Conventional /Once daily dosing:** **PRE:** 30 mins or just before next dose (to check for toxicity) *some cases may need Post2hr and Post6hr levels	**i) Conventional dosing:** Trough: < 2 **ii) Single Daily Dosing:** Trough: < 1 **iii)Neonates:** Trough: < 1	**i) Conventional dosing:** Trough: < 4.18 **ii) Single Daily Dosing:** Trough: < 2.1 **iii)Neonates:** Trough: < 2.09	2.09
Vancomycin	After 3rd dose (Excluding Loading dose) **ESRF/HD**: 24 hours after 1st dose / Just before HD	**Trough level monitoring** PRE: 30 mins or just before next dose **AUC24 Monitoring** PRE: 30 mins or just before next dose POST: 1 hour after completing of infusion **Continuous Infusion**: After 12-24 hours of starting of CI	**Peak:** 25-40 **Trough:** SSTI: 10-15 Deep Seated: 15-20 Neoate/Paed:10-20 HD/Cont.Inf: 15-25	**Peak:** 17.25- 27.6 **Trough:** SSTI: 6.9-10.35 Deep Seated: 10.4-13.8 Neonate/Paed: 6.9-13.8 HD/Cont.Inf: 10.4-17.3	0. 69
			AUC: 400-600mg.h/L		
Phenytoin	**With LD**: 12-24 hours **Without LD**: 7-10 days	**Loading dose**: Oral: 24 hours after administration of oral loading dose IV: 2 hours after completion of IV loading dose (to determine maintenance dose or need to reload.) PRE: Just before next dose *IF SUSPECT TOXICITY - Random level	10-20	40-80	3.96
Carbamazepine	**Initiation**: 2-3 weeks (Induction phase) **Maintenance dose**: 2 – 5 days (after dose adjustment)	PRE: Just before next dose	4 - 1 2	17-51	4.23
Valproic Acid	2 - 4 days	PRE: Just before next dose	50-100 *may go up to 125 for PSY, based on clinical condition	347-693 *may go up to 866 for PSY, based on clinical condition	6.93
Acetaminophen (Paracetamol)		At least 4 hours after ingestion (4 – 24 hours)	10-30	**No need conversion**	
Outsource to H. Selayang					
Amikacin	**SDD:** After 24 hours (Sample at least after 2 doses) **Conventional:** after 3rd dose	**Conventional /Once daily dosing:** PRE: 30 mins or just before next dose (to check for toxicity) *some cases may need Post2hr and Post6hr levels	**i) Conventional dosing:** Trough: <10 **ii) Single Daily Dosing:** Trough: <1 **iii)Neonates:** Trough: <5	**i) Conventional dosing:** Trough: <17.1 **ii) Single Daily Dosing:** Trough: <1.71 **iii)Neonates:** Trough: < 8.55	1.71
Digoxin	**Initiation dose:** **With LD:** 12- 24 hours **Without LD:** 3-5days **Maintenance dose:** 5-7 days after dose adjustment **(ESRF: 15 - 20 days)**	PRE: 30 mins or just before next dose i) Oral: If dose already taken, at least 6 hours post dose ii) IV: If dose already taken, at least 4 hours post dose	**CHF:** 0.5 – 0.9 **AF**: 0.8 – 2	**CHF**: 0.64 – 01.152 **AF**: 1.024 -2.56	1.28
Phenobarbitone	**Neonate:** 1 month **Infant/Children:** 2 weeks **Adult:** 1 month **Without LD:** 2 - 4 weeks (after the initiation/ a change in the regimen)	**Loading dose:** **2 -3 hours after administration** PRE: Just before next dose	15-40 (depend on indication)	65-172 (depend on indication)	4.31
Outsource to HKL					
Theophylline	**Premature neonate:** 6 days **Neonate:** 4 -7 days **Infant:** 1-5 days **Adult/Child:** 2 days	**With LD:** 30 min after end of infusion (to determine maintenance dose) **Continuous Infusion:** 12-24 hrs after administration **Oral (Rapid @ sustained release):** Pre: 30 mins or just before next dose	**Asthma/COPD:** 10 – 20 **Apnea / Bradycardia in Neonates:** 5 – 10 **Ventilator Weaning in Neonates:** 5 – 20	**Asthma / COPD:** 55.5 -111 **Apnea / Bradycardia in Neonates:** 27.8– 55.5 **Ventilator Weaning in Neonates:** 27.8 -111	5.55

AMINOGLYCOSIDE

(GENTAMICIN & AMIKACIN)

Peak for power, trough for safety
-- dose wisely, monitor closely, and protect the kidneys!

1. INITIATING DOSE

Calculate using Population PK

DETERMINE THE DOSING WEIGHT (KG)

1. Determine actual body weight (**ABW**)
2. Determine ideal body weight (**IBW**)
3. Determine to use either **ABW, IVW** or **Adjusted BW** for dosing weight based on:
   - If ABW/IBW is > 0.9 to < 1.2 = Use **ABW**
   - If ABW/IBW is > 1.2 = Use **Adjusted BW**
   - If ABW/IBW is > 0.75 to < 0.9 = Use **IBW**
   - If ABW/IBW is ≤ 0.75 = Use **ABW x 1.13**

$$IBW\ (Male) = 50kg + 0.9(Ht - 152cm)$$

$$IBW\ (Female) = 45.5kg + 0.9(Ht - 152cm)$$

$$Adjusted\ body\ weight = IBW + 0.4(ABW - IBW)$$

DETERMINE THE VOLUME OF DISTRIBUTION (VD)

Neonates	0.4 – 0.6 L/kg
Paediatrics	0.3 – 0.5 L/kg [
Adult	0.2 – 0.3 L/kg
Obesity (>30% over IBW)	0.26 [IBW + 0.4 (TBW – IBW)
Cystic fibrosis	0.35 L/kg

$$Vd\ (L) = Population\ Vd\ (L/kg) \times Dosing\ Weight\ (kg)$$

ESTIMATE ELIMINATION RATE CONSTANT (KE)

$$Ke\ (hr^{-1}) = \frac{CL(L/hr)}{Vd(L)}$$

OR

$$Ke = 0.01 + (CrCl \times 0.0024)$$

$$CL(L/hr) = CrCl(ml/min) \times \frac{60min}{1000ml}$$

$$CrCl(ml/min) = \frac{(140 - Age) \times BW \times 1.04\,(F) or 1.23\,(M)}{(Scr(umol/L)}$$

ESTIMATE DOSING INTERVAL (τ):

$$\tau(hr) = \frac{lnTargetC_{max}^{*} - lnTargetC_{min}^{*}}{ke}$$

ESTIMATE INITIAL DOSE BY DECIDING TARGET CMAX

$$InitialDose(mg) = TargetC_{max}(mg/L)^{*} \times Vd(L) \times (1 - e^{-Ke(\tau)})$$

*Refer last page for target conc.

ESTIMATE EXPECTED CMAX AND EXPECTED CMIN CONCENTRATION:

$$ExpC_{max} = \frac{Dose(mg)}{Vd\,(L) \times (1 - e^{-Ke\tau})}$$

τ = Dose interval (hours)

$$ExpC_{min} = ExpC_{max} \times e^{-Ke\tau}$$

τ = Dose interval (hours)

AMINOGLYCOSIDE

(GENTAMICIN & AMIKACIN)

2. ESTIMATING NEW DOSE FROM THE MEASURED CONCENTRATION

A. WHEN POST 2 HOUR (C2) & POST 6 HOUR (C6) CONC. AVAILABLE; (USUALLY FOR SDD)

ESTIMATE ELIMINATION RATE CONSTANT (KE)

$$Ke\left(hr^{-1}\right) = \frac{lnC_2 - lnC_6}{t_6 - t_2}$$

C_2: Post 2 hours concentration (mg/L)
C_6: Post 6 hours concentration (mg/L)

t_2: Post 2 hours sampling time
t_6: Post 6 hours sampling time

ESTIMATE THE EXPECTED CMAX CONCENTRATION AND EXPECTED CMIN CONCENTRATION

$$C_{max} = C_2 \times e^{Ket'}$$

t': Time interval between end of infusion & C_2 sampling

$$C_{min} = C_{max} \times e^{-Ke\tau}$$

τ = Dose interval (hours)

ESTIMATE HALF LIFE (T1/2)

$$t_{\frac{1}{2}}\,(hr) = \frac{0.693}{Ke(hr^{-1})}$$

DETERMINE THE VOLUME OF DISTRIBUTION (VD)

$$Vd(L) = \frac{Dose(mg)}{C_{max}\left(1 - e^{-Ke\tau}\right)}$$

τ = Dose interval (hours)

USING THE CALCULATED KE, ESTIMATE NEW DOSE

$$NewDose(mg) = C_{max}\,(mg/L) \times Vd(L) \times \left(1 - e^{-Ke\tau}\right)$$

τ = Dose interval (hours)

$$ExpC_{min} = C_{max} \times e^{-Ke\tau}$$

τ = Dose interval (hours)

CALCULATE THE DRUG FREE PERIOD (DFP)- FOR SDD ONLY

Ensure DFP within 2 – 8 hours. If exceeds 8 hours, consider adjust interval/dose

$$tMIC(hr) = \frac{lnCmax - lnMIC}{Ke}$$

Time to reach MIC concentration (hours)

MIC: depends on the MIC of the culture

$$DFP(hr) = \tau - tmax - tMIC$$

Tmax= infusion time

B. WHEN PRE & POST CONC. AVAILABLE; (USUALLY FOR CONVENTIONAL DOSE)

ESTIMATE ELIMINATION RATE CONSTANT (KE)

$$Ke\left(hr^{-1}\right) = \frac{lnC_{post} - lnC_{pre}}{\tau - (t_{post} - t_{pre})}$$

C_{pre}: Pre dose concentration (mg/L)
C_{post}: Post dose concentration (mg/L)

τ: Dose interval (hours)
t_{pre}: Pre dose sampling time
t_{post}: Post dose sampling time

ESTIMATE THE EXPECTED CMAX CONCENTRATION AND EXPECTED CMIN CONCENTRATION

$$C_{max} = C_{post} \times e^{Ke\tau'}$$

τ': Time interval between end of infusion & C_{post} sampling

$$C_{min} = C_{max} \times e^{-Ke\tau}$$

τ = Dose interval (hours)

ESTIMATE HALF LIFE (T1/2)

$$t_{\frac{1}{2}}\,(hr) = \frac{0.693}{Ke(hr^{-1})}$$

DETERMINE THE VOLUME OF DISTRIBUTION (VD)

$$Vd(L) = \frac{Dose(mg)}{C_{max}\left(1 - e^{-Ke\tau}\right)}$$

τ = Dose interval (hours)

USING THE CALCULATED KE, ESTIMATE NEW DOSE

$$NewDose(mg) = C_{max}\,(mg/L) \times Vd(L) \times \left(1 - e^{-Ke\tau}\right)$$

τ = Dose interval (hours)

$$ExpC_{min} = C_{max} \times e^{-Ke\tau}$$

τ = Dose interval (hours)

CALCULATE THE DRUG FREE PERIOD (DFP)- FOR SDD ONLY

Ensure DFP within 2 – 8 hours. If exceeds 8 hours, consider adjust interval/dose

$$tMIC(hr) = \frac{lnCmax - lnMIC}{Ke}$$

Time to reach MIC concentration (hours)

MIC: depends on the MIC of the culture

$$DFP(hr) = \tau - tmax - tMIC$$

Tmax= infusion time

C. WHEN ONLY TROUGH CONC. AVAILABLE;

- To refer vancomycin calculation section > **TROUGH LEVEL ONLY**

Target Concentration Range

Dosing	Gentamicin (mg/L)		Amikacin (mg/L)	
	TROUGH	PEAK	TROUGH	PEAK
Neonates	< 1	5 - 12	< 5	20 - 30
MDD	<2	5 - 10	<10	20 - 30
SDD	< 1	10 - 30*	< 1	60*
Synergy	< 1	3 - 5	N/A**	N/A**
Hemodialysis	<2	Not necessary	<10	Not necessary

*The target concentration ranges vary and may be individualized based on institutional MIC value to achieve peak to MIC ratio of 10:1

HOSPITAL SUNGAI BULOH
THE SKILL TO HEAL THE SPIRIT TO CARE
CEKAP MERAWAT PRIHATIN MENJAGA

PREPARED BY: TDM TEAM HSGB
NUR FARHANA, SITI SYARIHAN, CHLOE, , LIM WAI SHIN
UPDATED: 2/5/2025

VANCOMYCIN

**"Calculating vancomycin dose adjustments is easy
-just balance trough levels, renal function, and a bit of math. The key?
Precision, patience, and knowing your kinetics!"**

INITIATING DOSE

Calculate using Population PK

Creatinine Clearance, CrCl

$$CrCl = \frac{(140 - age) \times BW(kg) \times 1.04(F) or 1.23(M)}{SCr\,(umol/L)}$$

Elimination Rate Constant, Ke

$$Ke\left(hr^{-1}\right) = 0.0044 + 0.00083[CrCl(ml/min)]$$

Half-life, T1/2

$$T_{1/2} = \frac{ln2}{ke(h^{-1})}$$

Loading Dose, LD

$$LD = 25 - 30mg/kg/dose$$

Maintenance Dose, MD

C_{min} target

- MRSA Bacteremia (Unstable renal function) : 15-20mg/L
- CNS infection: 15-20mg/L
- SSTI or UTI: 10-15mg/L
- MRCONS or Enterococcus faecium: 10-20mg/L

Vd = 0.7 L/kg x BW (kg)

$$MD = \frac{C_{min}target \times Vd(L) \times (1 - e^{-KeT})}{e^{-KeT}}$$

T = interval (hr)

VANCOMYCIN

TROUGH LEVEL ONLY

Conversion factors : umol/L to mg/L ÷ 0.69
mg/L to umol/L x 0.69

Cmax

$$C_{max} = C_{trough} + \frac{Dose(mg)}{Vd(L)}$$

Vd = 0.7 L/kg x BW (kg)

Elimination Rate Constant, Ke

$$Ke = \frac{lnC_{max} - lnC_{min}}{T(h)}$$

T = interval (hr)

Half-life, T1/2

$$T_{1/2} = \frac{ln2}{ke(h^{-1})}$$

New Dose

Cmin target

- MRSA Bacteremia (Unstable renal function) : 15-20mg/L
- CNS infection: 15-20mg/L
- SSTI or UTI: 10-15mg/L
- MRCONS or Enterococcus faecium: 10-20mg/L

$$MD = \frac{C_{min}target \times Vd(L) \times (1 - e^{-KeT})}{e^{-KeT}}$$

Vd = 0.7 L/kg x BW (kg)

T = interval (hr)

Expected Cmax from New Dose

Vd = 0.7 L/kg x BW (kg)

$$ExpC_{max} = \frac{Newdose(mg)}{Vd(L) \times (1 - e^{-KeT})}$$

T = interval (hr)

Expected Cmin from New Dose

$$ExpC_{min} = C_{max} \times e^{-KeT}$$

T = interval (hr)

VANCOMYCIN

TROUGH & PEAK LEVEL

Conversion factors : umol/L to mg/L ÷ 0.69
mg/L to umol/L x 0.69

Elimination Rate Constant, Ke

$$Ke = \frac{lnC_{peak} - lnC_{trough}}{T - (t_2 - t_1)(h)}$$

- T = Interval
- t_2 = peak sampling time
- t_1 = trough sampling time

Half-life, T1/2

$$T_{1/2} = \frac{ln2}{ke(h^{-1})}$$

Cmax

$$C_{max} = C_{peak} \times e^{Ket'}$$

- t' = Interval between end of infusion & peak sampling time

Cmin

$$C_{min} = C_{max} \times e^{-Ke(T-t\`)}$$

- t` = Infusion time

AUC24 Calculation

Target AUC24 = 400 - 600 mg.h/L

Indication: MRSA Bacteremia

- Bacteremia
- Endocarditis
- Pneumonia
- Bone/ Joint Infection
- Neutropenic Fever

AUC Infusion

$$AUC_{inf} = t\` \times \frac{C_{max} + C_{min}}{2}$$

- t` = Infusion time

AUC Elimination

$$AUC_{elim} = \frac{C_{max} - C_{min}}{Ke}$$

AUC24

$$AUC_{24} = \frac{24}{T} \times (AUC_{inf} + AUC_{elim})$$

- T = Interval

New Total Daily Dose, New TDD

$$NewTDD = CurrentTDD \times \frac{AUC_{desired}}{AUC_{calculated}}$$

- AUC desired = 400 - 600 mg.h/L

Expected AUC24 from New Dose

$$ExpAUC_{24} = \frac{TDD_{newdose}}{TDD_{olddose}} \times AUC_{calculated}$$

Example:
TDD New Dose = 650mg QID = **2600mg**
TDD Old Dose = 750mg TDS = **2250mg**

BY: TDM TEAM (NUR FARHANA, SITI SYARIHAN, PRP ANIS)

ed April 2025

PHENYTOIN CALCULATION

1. To calculate Loading Dose (LD)

***Adult: 10-20mg/kg; Peads: 15-20mg/kg**

$$\text{Loading dose} = \frac{Cpdesired \times Vd \times BW}{S \times F}$$

- Vd: 0.7L/kg
- S: IV / Cap = 0.92; Susp = 1.0
- F: 1.0

2. To calculate Maintenance Dose (LMD)

$$\text{Maintenance dose} = \frac{Vmax \times BW \times Cp_{desired}(mg/L)}{S \times F \times (Km + Cp_{desired}(mg/L))}$$

- $Vmax$: 7mg/kg/day
- S: IV / Cap = 0.92; Susp = 1.0
- F: 1.0
- Km: 4mg/L
- $Cp_{desired}$: 10-20mg/L

3. To calculate expected Cpss from the given dose

$$\text{Cpss (mg/L)} = \frac{Km \times S \times F \times Dose\,(mg/day)}{(Vmax \times BW) - (S)(F)\,(Dose(mg/day))}$$

- Km: 4mg/L
- S: IV / Cap = 0.92; Susp = 1.0
- F: 1.0
- $Vmax$: 7mg/kg/day
- S: IV / Cap = 0.92; Susp = 1.0
- F: 1.0

4. To calculate Incremental LD

***when level is low and patient is clinically fitting**

$$\text{Incremental LD} = \frac{(Cp_{desired} - Cp_{measured}) \times Vd \times BW}{S \times F}$$

- $Cp_{desired}$: 10-20mg/L
- Vd: 0.7L/kg
- S: IV / Cap = 0.92; Susp = 1.0
- F: 1.0

5. To adjust dose based on measured Cpss

i. Calculate pt's Vmax

‼ calculate only when measured Cpss is a trough level

$$\text{Vmax (mg/day)} = \frac{S \times F \times Dose(mg/day) \times (Km + Cp_{measured})}{Cp_{measured}}$$

- S: IV / Cap = 0.92; Susp = 1.0
- F: 1.0
- Km: 4mg/L

i. Calculate new dose

$$\text{New Dose} = \frac{Vmax(mg/day) \times Cp_{target}}{S \times F \times (Km + Cp_{target})}$$

- $Vmax$: pt's Vmax
- Cp_{target}: 10-20mg/L
- S: IV / Cap = 0.92; Susp = 1.0
- F: 1.0
- Km: 4mg/L
- Cp_{target}: 10-20mg/L

PHENYTOIN CALCULATION

7. **To calculated corrected Phenytoin level due to hypoalbuminemia (Alb <25g/L)**

$$CpNormalBinding\,(mg/L) = \frac{Cp_{measured}\,(mg/L)}{\left[0.9 \times \frac{Pt's Albumin (g/L)}{44}\right] + 0.1}$$

8. **To calculated corrected Phenytoin level due to hypoalbuminemia (Alb <25g/L) and renal impairment (CrCl <10ml/min)**

$$CpNormalBinding\,(mg/L) = \frac{Cp_{measured}\,(mg/L)}{\left[0.9 \times 0.48 \times \frac{Pt's Albumin (g/L)}{44}\right] + 0.1}$$

9. **To calculate time to withold Phenytoin when the level is toxic**

*in the absence of other factors that would alter plasma binding (ie hypoalbuminemia, renal failure, other displacing drug)

$$\text{Time to withold (day)} = \left[Km\,(mg/L)\left(ln\frac{Cp_{measured}}{Cp_{desired}}\right) + (Cp_{measured} - Cp_{desired})\right] \times \frac{Vd\,(L)}{Vm\,(mg/day)}$$

0.7L/kg

4mg/L

10-20mg/L

10-20mg/L

pt's Vmax

BY: TDM TEAM (NUR FARHANA, SITI SYARIHAN)

ed March 2025

VALPROIC ACID *calculation*

1. To calculate Loading Dose

***recommended: 20-40mg/kg, max 3g**

50-100mg/L

Adult = 0.15 L/kg
Peads = 0.22 L/kg

$$\text{Dose (mg)} = \frac{Cp_{desired}\,(mg/L) \times Vd\,(L)}{S \times F}$$

1.0

IV / PO = 1.0
Sustained Release Tab = 0.9
Extended Release Tab = 0.8

2. To calculate Maintenance Dose

i. To calculate Clearance (Cl)

	Monotherapy	Polytherapy
Children	10-20ml/kg/hr	20-30ml/kg/hr
Adult	7-12ml/kg/hr	15-18ml/kg/hr

$$\text{Cl (L/hr)} = \frac{Cl\,(ml/kg/hr) \times BW\,(kg)}{1000ml}$$

ii. To volume of distribution (Vd)

Adult = 0.15 L/kg
Peads = 0.22 L/kg

$$\text{Vd (L)} = Vd\,(L/kg)\ x\ BW\,(kg)$$

iii. To calculate elimination rate constant (Ke (hr^{-1}))

$$\text{Ke } (hr^{-1}) = \frac{CL\,(L/hr)}{Vd\,(L)}$$

iv. To calculate half life (t1/2)

$$\text{t1/2} = \frac{0.693}{Ke\,(hr^{-1})}$$

v. To calculate maintenance dose

$$\text{Dose (mg)} = \frac{Cl(L/hr) \times Cpss_{desired}\,(mg/L) \times interval\,(hr)}{S \times F}$$

1.0

IV / PO = 1.0
Sustained Release Tab = 0.9
Extended Release Tab = 0.8

2. To adjust dose based on measured Cpss

i. To estimate clearance (Cl) from the measured concentration

Cl (L/hr) = $\dfrac{S \times F \times Dose\,(mg)}{Css_{measured} \times Interval\,(hr)}$

S: 1.0

F: IV / PO = 1.0; Sustained Release Tab = 0.9; Extended Release Tab = 0.8

ii. Determine the target Css and calculate new dose

Dose (mg) = $\dfrac{Cl(L/hr) \times Cpss_{desired}\,(mg/L) \times interval\,(hr)}{S \times F}$

S: 1.0

F: IV / PO = 1.0; Sustained Release Tab = 0.9; Extended Release Tab = 0.8

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