

AMIKACIN

01. Assay Details

[CH Labs Test Reference Guide](#)

02. Therapeutic Range

1. A 24-hour AUC of 150-200 mg/L.hr if using the target-AUC method (200 mg/L.hr if severe infection)
2. A 24-hour trough concentration of <2.0 mg/L if the AUC method not available

How well established:

Results from early studies in serious Gram-negative infections suggested that when using 6-12 hourly dosing, peak and trough concentrations should be 25-30 mg/L and <4-8 mg/L respectively. In the 1990's, evidence became available from animal and human studies that once-daily dosing of aminoglycosides is generally preferable to multiple daily administration. Over 30 clinical studies and at least 9 meta-analyses have now shown that once-daily administration is more effective than multiple-daily dosing and results in less nephrotoxicity. There is no significant difference in incidence of ototoxicity. Methodology for monitoring concentrations with once-daily administration is debated. In Christchurch, a target 24-hour area-under-the-concentration-time-curve (AUC) method has been developed as above with a target range of 150-200 mg/L.hr which is the AUC range expected with doses of 15-20 mg/kg/day in patients with normal renal function and average population values for volume of distribution and clearance. Although there is a sound theoretical basis for the target-AUC method of monitoring, the method has not been compared with other methods. A retrospective analysis of 100 patients treated with Gentamicin using the target-AUC method suggested that the method was practical, more appropriate than aiming for a trough concentration and toxicity was not greater than expected.

03. Pharmacokinetics

F: 0	Vd (L/kg): 0.3	Cl (L/h/kg): 0.1	t _{1/2} : 1.4 - 2.3 hrs
Fe: >0.9	Elimination route: Renal		
CYP: Nil	Protein binding: <0.11		

F = Bioavailability, Vd = volume of distribution, Cl = clearance, t_{1/2} = terminal half-life of elimination, Fe = fraction excreted unchanged in the urine, CYP = cytochrome P450 enzyme/s

Other PK data:

- Vd is increased in patients with severe burns or overwhelming infection (eg. ICU patients) and higher doses are likely to be required.

04. Indications

1. Gram-negative bacterial infection - including Pseudomonas, Proteus, Serratia, Klebsiella, E.coli.
2. Infections of bone, respiratory tract, skin, soft tissue, abdomen, urinary tract, and endocarditis, and septicaemia.

05. Loading Dose

8-20 mg/kg lean body weight according to the Table

Cal. CrCl (ml/min)	Dose in mg/kg	Time of second blood sample (hours)
>66	15–20 depending on the severity of infection	6-14
55-66	15	8-16
41-54	12	10-18
31-40	10	12-20
20-30	8	14-22
< 20	consider using another antibiotic	

$$\text{CrCl} = \frac{(140 - \text{age}) \times \text{lean body weight (kg)}}{\text{plasma creatinine (mmol/L)} \times 800} \quad (\times 0.85 \text{ if female})$$

lean body weight (kg) males = 50kg + 0.9kg for each cm > 150cm in height

lean body weight (kg) females = 45kg + 0.9kg for each cm > 150cm in height

Give the dose once-daily by IV infusion over 30 minutes in 100 ml saline.

Record the exact times of starting and finishing the infusion

Take 2 blood samples at 30 minutes after the end of the infusion and at between 6 and 22 hours after the infusion depending on renal function as in the Table

Record the exact time of blood samples

Contact the ward pharmacist or Clinical Pharmacology (Ext 80900) during normal working hours, with the concentration results to get a dose prediction for the next dose

06. Maintenance dose

Adjust the dose according to the calculated AUC as above aiming for an AUC between 150 and 200 mg/L.hr depending on the severity of infection.

07. Notes on administration

Give the dose once-daily by IV infusion over 30 minutes in 100ml 5% Dextrose

08. When to monitor

Refer to Loading Dose above. Repeat the 30 minute and 6-22 hour post-infusion blood samples every 3 days or prn depending on the clinical situation.

09. Dose individualisation

Adjust the dose according to the calculated AUC as above aiming for an AUC between 150 and 200 mg/L.hr depending on the severity of infection.

10. Adverse effects

1-10%

Nephrotoxicity
Neurotoxicity - vertigo, ataxia
Ototoxicity

<1%

CNS: drowsiness, headache, tremor, pseudotumour cerebri, neuromuscular blockade - in patients with a coexisting abnormality of neuromuscular transmission
CVS: hypotension
DERM: photosensitivity, erythema, alopecia, exfoliative dermatitis, purpura
GI: anorexia, nausea, vomiting
HAEM: eosinophilia
LIVER: elevated LFTs, hepatomegaly, hepatic necrosis
MUSC/SKEL: muscle cramps, weakness, arthralgia
RESP: dyspnoea
MISC: drug fever

11. Drug interactions

Increased nephrotoxicity can occur with concurrent:

diuretics, cephalosporins, piperacillin, amphotericin B, vancomycin, NSAIDs, tacrolimus, ciclosporin

Increased ototoxicity can occur with concurrent:

diuretics, carboplatin, other ototoxic agents

Neuromuscular blockade can be aggravated with other neuromuscular blocking agents

12. Factors that may give a false assay result

Nil known

13. Overdose

TOXINZ <https://www.toxinz.com/specifications/antibacterials---aminoglycosides/amikacin/?&name=Amikacin>

14. Dialysability

This is of questionable value.

Haemodialysis is preferred over peritoneal dialysis

15. Comments

Nil

16. Key references

1. Van der Auwera P. Pharmacokinetic evaluation of single daily dose amikacin. *Journal of Antimicrobial Chemotherapy* 1991; 27, suppl. C: 63-71.
2. Barclay ML, Kirkpatrick CMJ, and Begg EJ. Once daily aminoglycoside therapy; Is it less toxic than multiple daily doses and how should it be monitored? *Clin Pharmacokinet* 1999, 36(2): 89-98.
3. Drug Information Handbook.
4. Drug Dex Drug Evaluation.

17. Last updated

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