

Once daily gentamicin in adults

Key messages

- **Once daily dosing for all adult patients, except those with tetraplegia.** Use the Table (below) to ensure that the:
 - first dose is calculated appropriately to maximise bacterial kill and minimise toxicity
 - two blood samples for gentamicin concentrations are taken at the correct times to guide subsequent doses
- **Endocarditis treatment with gentamicin at CDHB is changing to once daily dosing (blue box).** Note that the:
 - first dose is 3 mg/kg once daily
 - two blood samples for gentamicin concentrations are taken at the 'peak' and at 6 – 12 hours post-dose
 - change in guidelines will not appear in the Pink Book until 2015
- Monitor renal function and hearing/vestibular function in all patients

Gentamicin is an aminoglycoside antibiotic used mainly to treat Gram-negative infections. Most indications (eg. UTI, sepsis) are treated with once daily dosing of 3 to 7 mg/kg/day depending on renal function, focus and severity of infection. Patients with *tetraplegia* (including T1 involvement) receive divided daily dosing to minimise the risk of respiratory compromise due to high peak gentamicin concentrations – see Pink Book (18th ed), 2014, p162. Synergistic dosing for endocarditis is discussed in the blue box below.

ONCE DAILY DOSING

Pink Book (18th ed) 2014, p161

Gentamicin produces its greatest bacterial kill from the first dose and the antibacterial effects are less with subsequent doses. For this reason, it is essential that the first dose is calculated appropriately after consideration of both renal function and ideal body weight – see Table below.

Table: Calculation of the first gentamicin dose

(not to be used for patients with tetraplegia or endocarditis)

CrCl (mL/min)	Dose in mg/kg (ideal body weight)	Time of second blood sample (hours)
> 66	5 – 7	6 – 14
55 – 66	5 – 6	8 – 16
41 – 54	5	10 – 18
31 – 40	4	12 – 20
20 – 30	3	14 – 22
< 20	Gentamicin not recommended	-

Ensure that two blood samples are taken:

- 30 minutes after the end of the infusion ('peak'), and
- 6 – 22 hours after the end of the infusion depending on creatinine clearance (CrCl) – see Table above.

These concentrations are used to predict future doses by aiming for a peak of 15 to 30 mg/L, a trough <0.5 mg/L and a 24 hour area under the concentration-time curve (AUC) of 70 to 100 mg/L.h (depending on severity of infection).

WHY ONCE DAILY DOSING INSTEAD OF DIVIDED DOSES?

1. **Concentration-dependent bacterial kill.** The higher the gentamicin peak concentration the greater the number of bacteria killed (this contrasts with β -lactams and vancomycin where time above the minimum inhibitory concentration (MIC) determines rate of kill).

2. **Post-antibiotic effect.** Gentamicin suppresses bacterial growth for 1 to 8 hours after the concentration falls below the MIC. Higher peak concentrations prolong this phenomenon.
3. **Adaptive resistance.** Bacteria exposed to gentamicin develop resistance that resolves when drug exposure declines. Once daily dosing helps minimise this adaptive resistance as gentamicin concentrations at the end of the dosing interval are very low.
4. **Toxicity.** Evidence shows that once daily gentamicin causes less nephrotoxicity than three times daily dosing with the same total daily dose. The evidence is less clear for ototoxicity though some data suggests an advantage for once daily dosing.

ONCE DAILY DOSING OF GENTAMICIN FOR ENDOCARDITIS IN ADULTS

A change to CDHB guidelines*

- Gentamicin is used for synergy with β -lactams in the treatment of some types of bacterial endocarditis.
- From April 2014, CDHB is changing from the current regimen of 1 mg/kg iv q8h (target peak concentration of 2 to 4 mg/L and trough < 1 mg/L) to once daily dosing based on increasing evidence to support this approach.
- The initial dose is 3 mg/kg (ideal body weight) once daily administered intravenously over 30 minutes in 100 mL of sodium chloride 0.9%. Consult Infectious Diseases if the patient's CrCl is < 20 mL/min.
- Prescribe on the Aminoglycoside Prescription/Monitoring Form (C160030) and write on the QMR0004 'see aminoglycoside chart'.
- Take TWO blood samples after the first dose:
 - 30 minutes after the end of the infusion
 - 6 – 12 hours after the end of the infusion
- Contact the Ward Pharmacist or Drug Information (ext. 80900) for advice around subsequent doses. Target AUC (24 hours) is usually 30 – 50 mg/L.h.

*The Pink Book will not be updated to reflect the new guidelines until 2015. Please refer to the Pharmacy Intranet ("Antimicrobial Stewardship") or the back of the new Aminoglycoside Prescription/Monitoring Form (C160030) for the new once daily dosing guidelines.