

Guidance on synergistic use of gentamicin in adults (age >16)

Background

All patients with suspected or proven endocarditis should be discussed with microbiology. This policy is intended for the management of endocarditis and not other indications where gentamicin may be used for synergistic purposes. Synergistic gentamicin is recommended in initial treatment of native valve endocarditis due to enterococcal and streptococcal species and in prosthetic valve endocarditis of all aetiology including staphylococci. The addition of gentamicin in staphylococcal native valve infective endocarditis (IE) is no longer recommended because it increases renal toxicity. Therapy should be discussed with an infection specialist to consider resistance, clinical response, toxicity and suitability for outpatient therapy.

Cautions

Take particular care:

- ❖ In patients with acute kidney failure ($\geq 50\%$ increase in baseline serum creatinine or oliguria > 6 hours in previous 48 hours)
- ❖ In patients with chronic kidney disease (CKD Stage 4 or more; eGFR less than 30ml/min/1.73m²)
- ❖ If creatinine is currently rising; ensure that creatinine result is up to date

Renal toxicity with gentamicin is more likely in septic patients, or those who are also on other potentially nephrotoxic drugs such as NSAIDs, ACE inhibitors or diuretics; regardless of initial creatinine clearance.

DOSAGE GUIDELINES

These guidelines aim to produce a 1 hour post dose peak of 3-5 mg/L and a trough of <1 mg/L. Higher peaks may be recommended by microbiology in patients with MSSA infection.

Doses should be administered by IV bolus injection over 3-5 minutes.

STEP 1: Calculate, Prescribe and Administer First Dose

1.1 Calculate renal function

Use: MAXIMUM BODY WEIGHT CREATININE CLEARANCE CALCULATOR

Available via Firstport: <http://www.medednhs.lanarkshire.nhs.uk/sites/phcalx/cockcroftgault-mbw.asp>

Patient age, actual body weight, height and serum creatinine are required for calculation

Note creatinine clearance from the calculator and then go to step 1.3 (Page 3) for dosing guidance

1.2 Alternative renal function manual calculation if online calculator unavailable

- ❖ Use instructions below to calculate renal function
- ❖ Obtain a second professional check for all calculations

A Determine the maximum body weight for patient using the table below

Table 1: Maximum body weight (MBW) table

Height (ft)	Height (cm)	Male (kg)	Female (kg)		Height (ft)	Height (cm)	Male (kg)	Female (kg)
4'8''	142	49	43		5'9''	175	85	79
4'9''	145	52	47		5'10''	178	88	82
4'10''	147	54	49		5'11''	180	90	85
4'11''	150	58	52		6'0''	183	94	88
5'0''	152	60	55		6'1''	185	96	90
5'1''	155	62	58		6'2''	188	98	94
5'2''	158	66	60		6'3''	191	101	97
5'3''	160	68	62		6'4''	193	104	99
5'4''	163	71	66		6'5''	195	107	101
5'5''	165	74	68		6'6''	198	109	105
5'6''	168	77	71		6'7''	201	113	108
5'7''	170	79	74		6'8''	203	115	110
5'8''	173	82	77					

B Is the patient's actual body weight less than the maximum body weight in the chart above

Yes: Use the actual body weight for calculating creatinine clearance

No: Use the maximum body weight from chart above for calculating creatinine clearance

C Calculate estimated creatinine clearance using the 'Cockcroft Gault' equation (Box 1)

Box 1: Estimation of creatinine clearance (CrCl)

$$\text{CrCl (ml/min)} = \frac{(140 - \text{age (years)}) \times \text{weight (kg)} \times 1.23 \text{ (male) or } 1.04 \text{ (female)}}{\text{Serum creatinine (micromol/L)}}$$

Cautions:

- ❖ Use actual body weight or maximum body weight whichever is lower.
- ❖ In patients with low creatinine (< 60 micromol/L), use 60 micromol/L.

1.3 Calculate initial dosing

Use table 2 below to calculate gentamicin dose

Use Creatinine clearance value from MAXIMUM BODY WEIGHT CREATININE CLEARANCE CALCULATOR OR manual calculation above (steps 1.1 OR 1.2)

- ❖ Dose is based on **actual body weight** and approximates to 1 mg/kg
- ❖ Doses are capped at **maximum of 120mg** to prevent overdosing in severely obese patients
- ❖ Dosage interval is based on calculated creatinine clearance

Table 2: Initial GENTAMICIN dose and dosing interval

Gentamicin Synergistic Dosing Guidelines	Patient Weight				
	< 45 kg	45-65 kg	66-85 kg	86-110 kg	>110 kg
Actual body weight/ Creatinine CL					
<25 ml/min	40 mg	60 mg	80 mg	100 mg	120 mg
	Take a sample after 24 hours. Do not give a further dose until the concentration is <1 mg/L				
25-44 ml/min	40 mg 24 hourly	60 mg 24 hourly	80 mg 24 hourly	100 mg 24 hourly	120 mg 24 hourly
>44 ml/min	40 mg 12 hourly	60 mg 12 hourly	80 mg 12 hourly	100 mg 12 hourly	120 mg 12 hourly

1.4 Prescribe on drug cardex and administer first dose

- ❖ Use the synergistic gentamicin prescribing, administration, monitoring form for adults to prescribe synergistic gentamicin
- ❖ Prescribe on drug cardex 'as per chart', clearly annotate 'synergistic gentamicin' in the indication box on the cardex

STEP 2: Monitor Gentamicin and Creatinine concentrations

Concentrations are meaningless unless the dose & sample time are recorded accurately

- ❖ Take a sample for peak level analysis one hour after the first dose
Target peak concentration 3-5mg/L
- ❖ Take a sample for trough level analysis immediately before the second dose, then give the next dose. Do not delay giving the second gentamicin dose while waiting for trough concentration. **Target trough concentration ≤ 1 mg/L**
- ❖ Adjust the dose if necessary and monitor serum levels daily until target peak and trough levels achieved.
- ❖ Once target levels achieved monitor trough levels every 2-3 days. Monitor creatinine daily.
- ❖ If CrCl < 45ml/min or renal function changing, continue to monitor trough levels daily and discuss with pharmacy.

- ❖ If the gentamicin trough concentration is >1 mg/L and a further dose has already been administered, take a further trough **before** the next dose is given. Do not give a further dose until the gentamicin concentration is <1 mg/L

Seek advice from Pharmacy or Microbiology if unsure how to interpret results or adjust the dose

GENTAMICIN DURATION

- ❖ Gentamicin therapy should continue for 2 weeks except on microbiology advice.

STEP 3: Monitoring for signs of toxicity

Gentamicin can cause renal toxicity and ototoxicity. The risk of gentamicin increases with duration of therapy. If more than 2 weeks of therapy is required please refer the patients to audiology for hearing tests.

Renal toxicity:

- ❖ Monitor creatinine daily.
- ❖ Seek advice if renal function is unstable (e.g. a change in creatinine of >15-20%)
- ❖ Signs of renal toxicity include an increase in creatinine or decrease in urine output/oliguria
- ❖ Consider an alternative agent if creatinine is rising or the patient becomes oliguric

Ototoxicity:

- ❖ Ototoxicity is independent of drug concentration. It is due to drug accumulation within the inner ear and is associated with prolonged aminoglycoside use (usually >10 days but may be >72 hours).
- ❖ Symptoms of ototoxicity include new tinnitus, dizziness, poor balance, hearing loss or oscillating vision.
- ❖ Stop treatment if ototoxicity is suspected and refer to a microbiology/infection specialist for advice on future therapy

Patients who expect to be on gentamicin therapy for over 3 days should be given a 'Gentamicin and your ears leaflet':

<http://firstport2/resources/patient-info-leaflets/Documents/PIL.GNTEAR.06725.L.pdf>