NHS Grampian

Guidance For Dosing And Monitoring Of Synergistic Gentamicin For Endocarditis In Adults By Prescribers Working Within NHS Grampian

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Signature:		**Signature:**

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Policy Statement:
It is the responsibility of all staff to ensure that they are working to the most up to date and relevant guideline, policies, protocols and procedures.

Version 2

Executive Sign-Off

This document has been endorsed by the Director of Pharmacy and Medicines Management

Signature: ______________________

Replaces: NHSG/Guid/SynGent/MGPG915, Version 1

Document application: NHS Grampian Acute

Revision History:

Revision Date	Summary of Changes	Changes Made
September 2023	Changed title and purpose/description to reflect content.	
September 2023	Updated advice on: when synergistic gentamicin in indicated when to discuss with microbiology or infection specialist.	Introduction – page 3
September 2023	Added advice on prescribing on HEPMA.	Prescribing – page 4
September 2023	Added information on concerns of deterioration renal function or signs of toxicity.	Monitoring – If Creatinine Clearance ≥25mL/min - page 4
September 2023	Added –'immediately before the next dose would be given- to bullet point 3 Added 'If the prescribed dose or frequency requires to be altered ensure this is updated and re-prescribed on the patient's medicine Prescription and Administration Record (PAR)/HEPMA.'	Monitoring –All patients - page 4
September 2023	Added advice on when microbiology or infection specialist should be consulted.	Gentamicin duration – page 5
September 2023	Added 'Discuss the ongoing need for gentamicin with microbiology/ID if the patient has signs of worsening renal function'	Toxicity - renal toxicity – page 6
September 2023	Added statement on advising patients to report signs of ototoxicity	Toxicity – ototoxicity- page 6
September 2023	Updated link to SAPG maximum body weight table	Estimation of creatinine clearance - page 6
September 2023	Added: • Record the exact time of ALL gentamicin samples on the request form.' • '(DO NOT DELAY DOSE)' • '(Check further troughs every 2-3 days)' if maintaining same dose. • Updated notes box.	Appendix 2 – Monitoring for creatinine clearance ≥ 25mL/min after 2nd sample.

Consultative Group

Name:	Title:
Dr Nicola Ryan (on behalf of all Consultant Cardiologists)	Consultant Cardiologist
Antimicrobial Management Team	Approved at July 2024 meeting

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Guidance For Dosing And Monitoring Of Synergistic Gentamicin For Endocarditis In Adults By Prescribers Working Within NHS Grampian

1. Introduction

Synergistic gentamicin is recommended in the initial empirical treatment of endocarditis and for some particular endocarditis pathogens, in accordance with current national guidelines. Refer to BNF for cautions, contraindications, etc.

All patients with suspected or proven endocarditis should be discussed with microbiology or an infection specialist within 72 hours **and** re-discussed after 2 weeks if continuation of gentamicin is being considered. Resistance, clinical response, toxicity and need for outpatient therapy via OPAT service should be considered.

The addition of gentamicin in staphylococcal native valve infective endocarditis (IE) is no longer recommended because it increases renal toxicity without evidence of additional benefit.

1.1. Objectives

To guide safe, appropriate dosing and monitoring of synergistic gentamicin in patients with endocarditis.

1.2. Patient Groups To Which This Document Applies

Adults in the acute sector prescribed synergistic gentamicin for the treatment of endocarditis.

1.3. Patient Groups To Which This Document Does Not Apply

Adults prescribed gentamicin for any indication outwith endocarditis. Paediatric patients.

2. Process Document Main Components And Recommendations

2.1. Dosage guidelines

These guidelines aim to produce a 1 hour post dose peak of 3-5mg/L and a trough of <1mg/L. Doses should be administered by slow intravenous (IV) bolus injection over 3-5 minutes.

GENTAMICIN SYNERGISTIC DOSING GUIDELINES						Gentamicin dosing recommendations
Creatinine Clearance*	**Patient Weight** (Actual body weight – kg)					
	<45kg	**45–65kg**	**66-85kg**	**86-110kg**	**>110kg**	
<25mL/min	40mg	60mg	80mg	100mg	120mg	
	Take a sample after 24 hours. Do not give a further dose until the concentration is <1mg/L					
25 – 44mL/min	40mg 24 hourly	60mg 24 hourly	80mg 24 hourly	100mg 24 hourly	120mg 24 hourly	
>44mL/min	40mg 12 hourly	60mg 12 hourly	80mg 12 hourly	100mg 12 hourly	120mg 12 hourly	

*see section 2.6 for calculation of creatinine clearance

2.2. Prescribing

Prescribe on the regular section of the NHSG Prescription and Administration Record (PAR) or as a regular prescription on HEPMA; **do not use the gentamicin once daily (Hartford) prescribing, administration & monitoring form** to prescribe synergistic gentamicin.

2.3. Monitoring (see Appendix 2 for monitoring algorithm)

If Creatinine Clearance ≥25mL/min

1. Take a blood sample for gentamicin analysis one hour after the **first** gentamicin bolus injection has been administered ("peak" sample).
2. Take a second blood sample for gentamicin analysis at the end of the first dosage interval (**immediately before second dose** "trough sample") then give the next dose. Do not delay giving the second gentamicin dose while waiting for trough concentration to be reported, unless there are concerns over deteriorating renal function or any signs of toxicity.
   - Record the exact time of **all** gentamicin samples on the sample request form.
   - If the gentamicin peak concentration is within the range of 3-5mg/L and the gentamicin trough is <1mg/L, continue the present dosage regimen.
   - If the gentamicin peak concentration is not within the target range of 3-5mg/L, or the trough concentration is >1mg/L refer to Appendix 2 and seek specialist advice if necessary.

If Creatinine Clearance <25mL/min

1. Take a blood sample for gentamicin analysis one hour after the **first** gentamicin bolus injection has been administered ("peak" sample).
2. Take a blood sample after 24 hours ("trough" sample).
3. If the gentamicin peak concentration is within the range of 3-5mg/L and the gentamicin trough is <1mg/L, give the same dose and re-measure again after 24 hours.
4. If trough >1mg/L re-measure again after 6 – 12 hours and do not give a further dose until <1mg/L.

All Patients

1. Seek advice from pharmacy if you are unsure how to interpret the result or if the concentrations are not within the ranges above (see notes in Appendix 2).
2. Monitor the patient's creatinine daily. If renal function is stable, check the gentamicin trough concentration every 2 – 3 days. If renal function deteriorates, check the trough daily. Discuss dose regimen with pharmacy.
3. If the gentamicin trough concentration is >1mg/L and a further dose has been administered, re-analyse the trough after the appropriate dosing interval (immediately before the next dose would be given). Do not give a further dose until the gentamicin concentration is <1mg/L.
4. If the prescribed dose or frequency requires to be altered ensure this is updated and re-prescribed on the patient's Prescription and Administration Record (PAR)/HEPMA.

2.4. Gentamicin Duration

Microbiology or an infection specialist should be consulted to advise on the duration of synergistic gentamicin at the following times:

- Within 72 hours of starting antibiotic therapy
- At 2 weeks of therapy if continuation of gentamicin is being considered
- If the patient is causing concern (e.g. failure to respond, evidence of toxicity; see below)
- If discharge/OPAT is being considered (**Note:** there are alternatives to synergistic gentamicin if patients are being discharged via OPAT).

In general, where indicated, synergistic gentamicin therapy should continue for 2 weeks except in the case of enterococcal infective endocarditis (IE) when it may be given for 2 - 6 weeks on microbiology advice.

2.5. Toxicity

Gentamicin can cause renal toxicity and ototoxicity (cochlear and vestibular). The risk of gentamicin toxicity increases with duration of therapy. If gentamicin continues for >7 days, suggest referring to audiology for assessment.

Renal Toxicity

- Monitor creatinine daily. Seek senior medical advice if renal function is unstable (e.g. a change in creatinine of >15-20%).
- Discuss the ongoing need for gentamicin with microbiology/ID if the patient has signs of worsening renal function.
- 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 secondary to gentamicin is independent of drug concentration. It is suggested by any of the following: new tinnitus, dizziness, poor balance, hearing loss or oscillating vision.
- Patients prescribed gentamicin should be advised to report signs of ototoxicity. They should be asked about any signs and symptoms of ototoxicity regularly and this should be documented in the case notes.
- Toxicity is associated with prolonged aminoglycoside use (usually >7 days) and is secondary to drug accumulation within the inner ear.
- Stop treatment if ototoxicity is suspected and refer to a microbiology/infection specialist for advice on future therapy.

2.6. Estimation of Creatinine Clearance (CrCl)

The following 'Cockcroft Gault' equation can be used to estimate creatinine clearance (CrCl):

$$\text{CrCl (mL/min)} = \frac{[140 - \text{age (years)}] \times \text{weight}^{*}\text{ (kg)}}{\text{serum creatinine}^{\Delta}\text{ (micromol / L)}} \times 1.23 \text{ (male) } \textit{or}\ 1.04 \text{ (female)}$$

Cautions:

- *Use actual body weight or maximum body weight for patient's height, whichever is lower. For maximum body weight see Appendix 1 or: https://www.sapg.scot/media/4471/maximum-body-weight-table.pdf
- ΔIn patients with low creatinine (<60micromol/L), use 60 micromol/L to avoid overestimating creatinine clearance due to low muscle mass.
- Note: Use of estimated glomerular filtration rate (eGFR) from labs is **not** recommended for calculation of gentamicin doses.

3. References

Adapted from NHS GG&C guidelines approved for national adoption by the Scottish Antimicrobial Prescribing Group.

NHS GG&C Guidelines: Synergistic Gentamicin for Endocarditis in Adults 2019

4. Responsibilities For Implementation

Organisational:	Chief Executive and Management Teams
Corporate:	Senior Managers
Departmental:	Heads of Service/Clinical Leads
Area:	Line Managers
Hospital/Interface services:	Group Clinical Directors
Operational Management Unit:	Unit Operational Managers

Appendix 1: Maximum Body Weight Table – For Creatinine Clearance Calculations

This table can be used to determine whether patients are classed as 'obese' (>20% over Ideal Body Weight) and to determine the Maximum Body Weight for use in the Cockcroft Gault equation

Maximum Body Weight (MBW) table (= Ideal Body Weight + 20%)			
Height (ft inches)	**Height (cm)**	**MBW (kg) MALE**	**MBW (kg) FEMALE**
4' 8"	142	49	43
4' 9"	145	52	47
4' 10"	147	54	49
4' 11"	150	58	52
5' 0"	152	60	55
5' 1"	155	62	58
5' 2"	158	66	60
5' 3"	160	68	62
5' 4"	163	71	66
5' 5"	165	74	68
5' 6"	168	77	71
5' 7"	170	79	74
5' 8"	173	82	77
5' 9"	175	85	79
5' 10"	178	88	82
5' 11"	180	90	85
6' 0"	183	94	88
6' 1"	185	96	90
6' 2"	188	98	94
6' 3"	191	101	97
6' 4"	193	104	99
6' 5"	195	107	101
6'6"	198	109	105
6' 7"	201	113	108
6' 8"	203	115	110

Appendix 2: Synergistic Gentamicin In Endocarditis - Monitoring Algorithm

Record the exact time of ALL gentamicin samples on the request form.

TIME TO TAKE SAMPLE AFTER INITIAL DOSE

ACTION TO TAKE DEPENDING ON RESULTS OF **INITIAL** LEVELS

Patient Creatinine Clearance

- <25mL/min
  - Take 1st sample (Peak) **one hour after** bolus dose administered
    - Take 2nd sample (Trough) after 24 hours
      - If <**1mg/L** give same dose & re-measure again after 24 hours
      - If ≥**1mg/L** re-measure again after 6-12 hours & do **not** give a further dose until <1mg/L
- 25-44mL/min
- >44mL/min
  - Take 1st sample (Peak) **one hour after** bolus dose administered
    - Take 2nd sample (Trough) immediately **before next dose** is due & **give next dose** (DO NOT DELAY DOSE WHILE WAITING FOR TROUGH)
      - If Peak (1st sample) is **3-5mg/L** **AND** Trough (2nd sample) is **<1mg/L**
        Maintain **same** dosage regimen (Check further troughs every 2-3 days).
      - If Peak (1st sample) is **<3** or **>5mg/L** **AND/ OR** Trough (2nd sample) is **>1mg/L**
        →Seek advice (see notes below)

Monitor for Adverse Effects
Monitor creatinine daily. Seek senior medical advice if renal function is unstable (e.g. a change in creatinine of > 15-20%). Be alert for other signs of nephrotoxicity or ototoxicity.

Notes:
If levels are outwith the expected range, discuss required dose amendments with a specialist experienced in the use of synergistic gentamicin (e.g. Cardiology pharmacist/Senior medical staff, Antimicrobial pharmacist, Duty Microbiologist or Infectious Diseases senior medical staff).

If the trough level is >1mg/L: withhold further doses of gentamicin and monitor renal function closely.
Do not restart until plasma levels are <1mg/L **and** adjust dosing interval.

If the peak level is <3 or >5: Dose adjustment is required.

If a deterioration in renal function is seen, specialist advice should be sought regarding the safety of continuing gentamicin treatment.