NHS Grampian

NHS Grampian Guideline: Synergistic Gentamicin For Endocarditis In Adults

Co-ordinators:	Consultation Group:	Approver:
Specialist Antibiotic Pharmacists Specialist Cardiology Pharmacist	Antimicrobial Management Team Cardiology Team	Medicine Guidelines and Policies Group

Signature:		Signature:
Fiona McDonald S. Britton Lyle Dunn		Sandy Thorne

Identifier:	Review Date:	Date Approved:
NHSG/Guid/SynGent/ MGPG915	April 2020	April 2017

Uncontrolled when printed

Version 1

Executive Sign-Off

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

Signature: _____

Title: NHS Grampian Guideline: Synergistic Gentamicin For Endocarditis In Adults

Unique Identifier: NHSG/Guid/SynGent/MGPG915

Replaces: N/A – New Document

Across NHS Boards	Organisation Wide	Directorate	Clinical Service	Sub Department Area

Lead Author/Co-ordinator: Specialist Antibiotic Pharmacists, Specialist Cardiology Pharmacist

Subject (as per document registration categories): Prescribing Guideline

Key word(s): Guideline renal toxicity ototoxicity synergistic dosing creatinine clearance calculations gentamicin endocarditis

Process Document: Policy, Protocol, Procedure or Guideline Guideline

Document application: NHS Grampian

Purpose/description: To guide safe, appropriate prescribing and monitoring of synergistic gentamicin in patients with endocarditis.

Responsibilities for implementation:

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

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

Review: This policy will be reviewed in three years or sooner if current treatment recommendations change.

This document is also available in large print and other formats and languages, upon request. Please call NHS Grampian Corporate Communications on (01224) 551116 or (01224) 552245.

Responsibilities for review of this document:	Specialist Antibiotic Pharmacists
Responsibilities for ensuring registration of this document on the NHS Grampian Information/Document Silo:	Development Pharmacist – Medicines Management
Physical location of the original of this document:	Pharmacy and Medicines Directorate, Westholme
Job/group title of those who have control over this document:	Antimicrobial Management Team
Responsibilities for disseminating document as per distribution list:	Specialist Antibiotic Pharmacists

Revision History:

Revision Date	Previous Revision Date	Summary of Changes (Descriptive summary of the changes made)	Changes Marked* (Identify page numbers and section heading)
N/A	N/A	New Document	

* Changes marked should detail the section(s) of the document that have been amended i.e. page number and section heading.

NHS Grampian Guideline: Synergistic Gentamicin For Endocarditis In Adults

Contents Page No

NHS Grampian Guideline: Synergistic Gentamicin For Endocarditis In Adults

Introduction

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. Refer to BNF for cautions, contraindications, etc.

All patients with suspected or proven endocarditis should be discussed with microbiology or an infection specialist and resistance, clinical response, toxicity and need for outpatient therapy should be considered.

The addition of gentamicin in staphylococcal native valve infective endocarditis (IE) is no longer recommended because it increases renal toxicity.

These guidelines have been developed by NHS Greater Glasgow & Clyde and approved for national adoption by the Scottish Antimicrobial Prescribing Group.

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. 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)					
	< 45 kg	**45–65 kg**	**66-85 kg**	**86-110 kg**	**>110 kg**	
< 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 <1mg/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	

*see p4 for calculation of creatinine clearance

Prescribing

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

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 ("trough sample") then give the next dose. Do not delay giving the second gentamicin dose while waiting for trough concentration.
   - Record the exact time of **all** gentamicin samples on the sample request form.
   - If the gentamicin peak concentration is within the range of 3-5 mg/L and the gentamicin trough is <1 mg/L, continue the present dosage regimen.
   - If the gentamicin peak concentration is not within the target range of 3-5 mg/L, or the trough concentration is >1 mg/L. Discuss dose regimen with pharmacy (see notes in Appendix 2).

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 3-5 mg/L and the gentamicin trough is <1 mg/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 >1 mg/L and a further dose has been administered, re-analyse the trough after the appropriate dosing interval. Do not give a further dose until the gentamicin concentration is <1 mg/L.

Gentamicin Duration

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.

Toxicity

Gentamicin can cause renal toxicity and ototoxicity. 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%).
- 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.
- Toxicity is associated with prolonged aminoglycoside use (usually >10 days but may be >72 hours) 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.

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: http://www.scottishmedicines.org.uk/files/sapg/Maximum_body_weight_table.pdf
- $^{\Delta}$In 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.

For further advice contact:
Antibiotic Pharmacists Bleep 2937 Ext: 51048.
Clinical Pharmacists - see ward information for contact details.
Medical Microbiology bleep 2321 or contact switchboard.

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

Consultation:
Cardiology Team, NHS Grampian
Antimicrobial Management Team, NHS Grampian

References:
1. NHS GG&C Guidelines: Synergistic Gentamicin for Endocarditis in Adults 2017

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

Patient Creatinine Clearance

<25mL/min | 25-44mL/min | >44mL/min

TIME TO TAKE SAMPLE AFTER INITIAL DOSE

Take 1st sample (Peak) **one hour after** bolus dose administered

Take 2nd sample (Trough) after 24 hours

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

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

Take 1st sample (Peak) **one hour after** bolus dose administered

Take 2nd sample (Trough) immediately **before next dose** is due & **give next dose**

If Peak (1st sample) is **3-5mg/L**
AND
Trough (2nd sample) is **<1mg/L**

Maintain **same** dosage regimen

If Peak (1st sample) is **<3** or **>5mg/L**
AND/ OR
Trough (2nd sample) is **>1mg/L**

➔Seek advice from Pharmacy (see notes below)

Notes – advice on potential actions pending advice from Pharmacy:

If peak is >5 & trough <1 ➔ reduce dose and maintain same dosing interval

If peak is > 5 & trough >1 ➔ consider reducing the dose and/ or extending the dosing interval

If peak is < 3 & trough < 1 ➔ increase dose and maintain same dosing interval

If peak is <3 & trough >1 ➔ increase dose and extend the dosing interval

If peak is 3-5 & trough >1 ➔ increase the dosing interval

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.