NHS Dumfries & Galloway Guidelines: Synergistic Gentamicin for Endocarditis in Adults

ALL patients with suspected or proven infective endocarditis (IE) should be discussed with microbiology or Infectious Diseases (ID) within 72 hours of starting antibiotic therapy AND re-discussed after 2 weeks if continuation of gentamicin is being considered.

GENTAMICIN IS CONTRAINDICATED IN MYASTHENIA GRAVIS

Synergistic gentamicin is recommended in the initial empirical treatment of endocarditis and for some particular endocarditis pathogens, in accordance with national guidelines. When treating a patient with IE remember to consider resistance, clinical response, toxicity and suitability for outpatient parenteral antibiotic therapy (OPAT).

1. Initial Dosage Guidelines

These guidelines aim to produce a 1 hour post dose "peak" concentration of 3-5 mg/L, and an end of dosage interval "trough" concentration of <1 mg/L. **Doses should be administered by IV bolus injection over 3-5 minutes.**

Gentamicin: Synergistic Dosage Guidelines

	Patient Actual Body Weight				
Creatinine Clearance* (DO NOT use eGFR)	**<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 <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

** If creatinine is not known: give 1 mg/kg gentamicin (maximum 120 mg) and seek advice from pharmacy.*

DO NOT use eGFR: *creatinine clearance must be calculated.*

Adapted from GGC/SAPG policy by Susan Coyle, Antimicrobials Pharmacist. Approved by AMT and ADTC August 2021. Minor Amendment: August 2023. For review August 2024.

2. Prescribing

Prescribe on the HEPMA stating the dose and dose times; **do <u>NOT</u> use the (maroon) standard 'Adult Parenteral Gentamicin (GGC): Prescribing, Administration & Monitoring Chart' to prescribe *synergistic* gentamicin**. The 'Adult Parenteral Synergistic Gentamicin (GGC): Administration & Monitoring Chart' (see Appendix below) should be printed out and put with the patient's medicine Kardex to allow accurate recording of dose and sample times; this is ESSENTIAL for the correct interpretation of gentamicin concentration results. This chart must **NOT** be used as a prescription chart; doses and dose times must be prescribed on HEPMA.

3. Monitoring

1. Take a first blood sample for gentamicin analysis one hour after the first gentamicin bolus injection has been administered (a "peak" sample). At the first dose, the concentration may not yet be at steady state, and any repeat peak concentration measurements may be higher than the first.
2. Take a second blood sample for gentamicin analysis at the end of the first dosage interval (a "trough" sample) then give the next dose. **Do NOT delay giving the second gentamicin dose while waiting for the trough concentration to be reported, unless there are concerns over deteriorating renal function.**
3. 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 (dose amount and dose frequency).
4. Seek advice from pharmacy if you are unsure how to interpret the results or if the concentrations are not within the target ranges above.
5. If the gentamicin trough concentration is ≥1 mg/L and a further dose has already been administered, re-analyse the trough and await the result before re-dosing. **Do <u>NOT</u> give a further dose until the gentamicin concentration is <1 mg/L**.
6. If the prescribed dose amount/dose frequency is altered ensure this is updated and prescribed on HEPMA.
7. Record the exact time of all gentamicin samples on the Synergistic Gentamicin Administration and Monitoring Chart (see Appendix below).
8. Monitor the patient's creatinine daily and record this on the Synergistic Gentamicin Administration and Monitoring Chart (see Appendix below). If renal function is stable, check the gentamicin trough concentration every 2 days. If renal function deteriorates, or if the concentrations measured are not within the target range, check the trough concentration daily and discuss the dosage regimen with pharmacy.

4. Duration of Synergistic Gentamicin

Microbiology or ID 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 (N.B. there are alternatives to synergistic gentamicin if patients are being discharged via OPAT)

In general, synergistic gentamicin therapy should continue for 2 weeks except in the case of enterococcal IE, when it may be given for 2-6 weeks on microbiology/ID advice. The addition of synergistic gentamicin in staphylococcal **native valve** IE is no longer recommended as it increases renal toxicity without evidence of additional benefit.

5. Toxicity

Gentamicin can cause nephrotoxicity and ototoxicity (cochlear and vestibular). The risk of gentamicin toxicity increases with increasing duration of therapy.

Nephrotoxicity

- Monitor creatinine daily. Seek advice from pharmacy if renal function is unstable (e.g. a change in creatinine of >15-20%).
- Be alert for and react to any signs of renal toxicity e.g. increasing creatinine, decreased urine output/oliguria.
- Discuss the ongoing need for gentamicin with microbiology/ID if the patient has signs of worsening renal function.

Ototoxicity

- Gentamicin-induced ototoxicity occurs independently of drug concentration.
- Toxicity is associated with prolonged gentamicin use (usually >7 days) and is secondary to accumulation of drug within the inner ear.
- Ototoxicity is suggested by any of the following: new tinnitus, dizziness, poor balance, hearing loss, oscillating vision.
- Patients prescribed gentamicin should be advised to report signs of ototoxicity (see below regarding the Patient Information Leaflet which should be issued to the patient). They should be asked about any signs and symptoms of ototoxicity regularly and this should be documented in the case notes.
- If gentamicin continues for >7 days the patient should be referred to audiology for ongoing audiometry testing.
- If ototoxicity is suspected **STOP** gentamicin treatment and refer to microbiology/ID for advice on ongoing therapy.

6. Gentamicin Patient Information Leaflet

Patients prescribed synergistic gentamicin should be given a copy of the NHS Dumfries & Galloway Gentamicin Patient Information Leaflet about in(see Appendix below) at the earliest opportunity. This should be documented in the relevant section of the Synergistic Gentamicin Administration and Monitoring Chart (see Appendix below).

Appendices

Adult Parenteral Synergistic Gentamicin (GGC): Administration & Monitoring Chart

&

NHS Dumfries & Galloway Gentamicin Patient Information Leaflet: 'Gentamicin and your ears'

http://hippo.citrix.dghealth.scot.nhs.uk/sorce/apps/sorce_doc_manager/Actions/view_doc.aspx?docid=1029289&revid=1031670

Adapted from GGC/SAPG policy by Susan Coyle, Antimicrobials Pharmacist. Approved by AMT and ADTC August 2021. Minor Amendment: August 2023. For review August 2024.

ADULT PARENTERAL SYNERGISTIC GENTAMICIN (GGC): ADMINISTRATION & MONITORING CHART

Refer to full 'Synergistic Gentamicin for Endocarditis in Adults' guideline for more information. All patients with suspected or proven endocarditis should be discussed with an infection specialist.

Patient name: ……

Date of birth: ……

CHI no.: ……

Affix patient label

Gentamicin Patient Information Leaflet issued to:
Patient ❑ on ……../……../……..
Other ❑_____on ……../……../……..
Issued by _____

Signs of gentamicin toxicity
Renal: ↓urine output/oliguria or ↑creatinine
Oto/vestibular: NEW tinnitus, dizziness, poor balance, hearing loss, oscillating vision

Toxicity may occur irrespective of gentamicin concentration

Step 1: Calculate the initial dose of gentamicin from the dosage table below:

	Patient Actual Body Weight				
Creatinine Clearance* (DO NOT use eGFR)	**<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 <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

**If creatinine is not known: give 1 mg/kg gentamicin (maximum 120 mg) and seek advice from pharmacy.*
DO NOT use eGFR: *creatinine clearance must be calculated*

Step 2: Prescribe the initial dose of gentamicin on the patient's medicine Kardex, ensuring that the gentamicin dose, frequency and dosage time are clear

- Record the indication and intended duration in the patient's medical notes.

Step 3: Administration & Monitoring (record using the chart overleaf)

- Administer each synergistic gentamicin dose as an intravenous bolus injection over 3-5 minutes and record the exact time of ALL gentamicin doses overleaf on this monitoring chart. Ensure that each dose is also charted on HEPMA
- Take a 'peak' level 1 hour after the first gentamicin bolus dose. The recommended target peak level is 3-5 mg/L. Record the exact time of ALL gentamicin samples overleaf on this monitoring chart.
- Take a 'trough' level before the second gentamicin dose (i.e. at the end of the dosage interval) but **DO NOT** await the result before re-dosing unless there are concerns about deteriorating renal function. The recommended target trough level is <1 mg/L.
- Thereafter repeat a gentamicin trough concentration at least every 2 days or daily if renal function deteriorates or if measured concentrations are not within target range.
- Seek advice from pharmacy if you are unsure how to interpret the result or if the concentrations measured are not within the recommended ranges above.
- If the prescribed dose or dose frequency is altered ensure this is updated and prescribed on HEPMA.

Step 4: Assess daily: the ongoing need for gentamicin and for signs of toxicity

- Issue the NHS Dumfries & Galloway patient leaflet "Gentamicin and you ears" to the patient and record this in the relevant section above.
- Gentamicin can cause renal toxicity (see above). Monitor & record creatinine daily on the monitoring chart. Discuss with microbiology/ID if renal function is worsening.
- Gentamicin can cause ototoxicity (see above). Patients should be asked about signs of ototoxicity regularly and this should be documented in the casenotes. Patients should be referred to audiology for assessment if gentamicin continues for >7 days and re-discussed with microbiology/ID if it continues for >14 days.

Patient name: ………………………………………………… **CHI no.:** ……………………………………………………………

TOXICITY **(see overleaf)** **Renal** & **Oto-vestibular Function** should be reviewed daily	**Gentamicin Administration Record** Complete each time gentamicin is administered (**as well as charting on HEPMA**.)				**Gentamicin Monitoring Record** To be completed by ALL staff taking blood for gentamicin concentration monitoring. **Record ALL sample dates/ times accurately below.**				
	Date given	Gentamicin dose (mg) ***Bolus over 3-5 mins***	Time given (24 hour clock)	Given by	Date of sample	Time of sample (24 hour clock)	Blood sample taken by PRINT name and status	Result (mg/L)	Action/ Comment
Cr = **micromol /L**				Sig 1: Sig 2:					
Cr = **micromol /L**				Sig 1: Sig 2:					
Cr = **micromol /L**				Sig 1: Sig 2:					
Cr = **micromol /L**				Sig 1: Sig 2:					
Cr = **micromol /L**				Sig 1: Sig 2:					
Cr = **micromol /L**				Sig 1: Sig 2:					
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Cr = **micromol /L**				Sig 1: Sig 2:					
Cr = **micromol /L**				Sig 1: Sig 2:					

Gentamicin and your ears

INFORMATION FOR PATIENTS & CARERS

Information for patients on Gentamicin for more than 3 days.

What is gentamicin used for?

Gentamicin is an antibiotic used for serious bacterial infections. It is prescribed for you because it is the most suitable choice to treat the type of bacteria causing your infection.

How is gentamicin given?

Gentamicin is given into a vein, either by injection or as a drip. It is usually given in hospital and the dose is calculated according to your age, height, weight and kidney function and also the severity and type of infection we are treating.

How can gentamicin affect my ears?

All medicines can have side effects and gentamicin is no exception.
Gentamicin can occasionally cause damage to the ears, which may show itself as dizziness, hearing loss, tinnitus (ringing in the ears) or difficulties with balance. If you develop any of these signs when you are on gentamicin, or shortly after finishing a course of gentamicin, please let your doctor know as soon as you can.
It is difficult to estimate the risk of these effects for an individual patient as it depends on several factors. The risk does increase if you are given a longer course of gentamicin so we will ask our colleagues in the audiology department to check your ears if we prescribe gentamicin for more than a few days.

What is done to reduce the likelihood that these effects will happen?

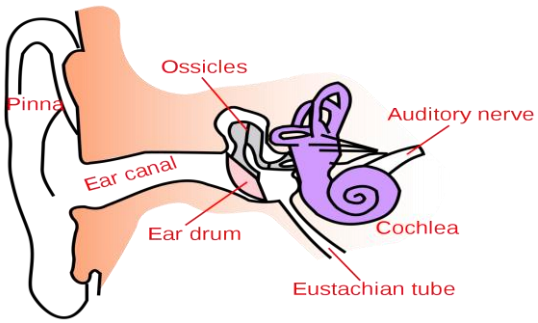
We will only use gentamicin for longer than a few days when it is necessary and we will discuss the risks and benefits of the treatment with you. We will take blood tests to check your kidney function before and during treatment and we will regularly measure the levels of gentamicin in your blood. Unfortunately the adverse effects on the ears can occur even when the blood levels are in the recommended range, so we cannot guarantee that they will not happen to you.

Is there anything I can do?

We would ask that you let us know immediately if you begin to feel dizzy or unsteady, have a deterioration in your hearing or ringing or buzzing in your ears. Please also tell us if you are taking any herbal or over-the-counter medicines so we can check that they are safe with gentamicin.

What if I have more questions?

Please speak to a member of the staff looking after you. If they cannot directly answer your Question, they will ask a colleague to help.



Further information contact: Susan Coyle Ext 32155 (Antimicrobial Pharmacist) or by E-Mail susan.coyle@nhs.net

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