NHS FORTH VALLEY

Guidelines for the use of Synergistic Gentamicin for Infective Endocarditis in Adults

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Consultation and Change Record – for All documents

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1. Introduction:

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

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

This guideline does not apply to:

- Patients requiring full treatment dose (non-synergistic) gentamicin - refer to the gentamicin dosing calculator, prescription chart and antimicrobial guidelines for information on full treatment dose gentamicin See: Right Decision Service

For the following patient groups discuss the suitability of gentamicin with microbiology or infectious diseases **before** starting it (**do NOT delay** initiating any other appropriate antibiotics pending this discussion about gentamicin)

- Patients treated in renal units or receiving renal replacement therapies
- Major burns
- Ascites
- Cystic fibrosis

Contraindications (see the BNF/product literature for full details)

- hypersensitivity
- myasthenia gravis
- patients who have previously experienced vestibular or auditory toxicity whilst on aminoglycosides
- patients with known family history of aminoglycoside induced auditory toxicity or a maternal relative with deafness due to mitochondrial mutation m.1555A>G
- patients with a known mitochondrial mutation
- decompensated liver disease (jaundice, ascites, encephalopathy, variceal bleeding or hepatorenal syndrome).

Cautions (see the BNF/product literature for full details)

- CrCl <21 ml/min, ≥50% increase in serum creatinine or oliguria for >6 hours in the past 48 hours
- If gentamicin is clinically indicated, give one dose as per guidance and check with microbiology, infectious diseases or pharmacy before giving a second dose, ensuring a trough concentration and renal function are checked.
- Patients with pre-existing auditory, vestibular impairment
- Co-administration with neurotoxic or nephrotoxic agents, e.g. neuromuscular blockers, nonsteroidal anti-inflammatory drugs, ACE Inhibitors; potent diuretics (i.e. IV diuretics, PO furosemide >80mg/daily, PO bumetanide >2mg/day, combination diuretics e.g. furosemide + metolazone), other aminoglycosides (see BNF (British National Formulary) | NICE)
- Patients with known conditions characterised by muscular weakness

2. Initial Dosage Guidelines

These guidelines aim to produce a 1-hour post dose "peak" concentration of between 10-12 mg/L, and an end of dosage interval "trough" concentration of <1 mg/L. The dose should be selected from the weight banded dosing in the table below. Doses **must** be calculated using maximum body weight if patients are obese (actual weight more than 20% above Ideal Body Weight) - see maximum body weight table.

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

Gentamicin: Synergistic Dosage Guidelines

Weight [Use ABW (or MBW if obese – see last page)]	ONCE DAILY Dose of Gentamicin
43kg to 49kg	140mg
50kg to 56kg	160mg
57kg to 64kg	180mg
65kg to 70kg	200mg
71kg to 76kg	220mg
≥77kg	240mg

If the patient is already receiving full treatment dose gentamicin and is to switch to synergistic dosing

- If renal function is stable **and** a gentamicin concentration taken in the past 48 hours is within the range expected for the current full treatment dose regimen then switch to once daily synergistic dosing when the next dose of gentamicin is due.
- If renal function is not stable **or** there are no gentamicin concentration results in the past 48 hours, then confirm that the patient's gentamicin concentration is <1mg/L before switching to synergistic dosing.

3. Prescribing

On HEPMA prescribe as 'Gentamicin IV STAT / Endocarditis / Synergy / Nebulised' Enter the dose, dosage frequency and intended duration (if known) on HEPMA.

The 'Adult Parenteral Synergistic Gentamicin Administration & Monitoring Chart' (Turquoise) should be printed out and used on the ward for accurate recording of administration and sample times; this is **essential** for the correct interpretation of gentamicin concentration results. Doses and dose times **must** be prescribed on HEPMA and amended on HEPMA if the dose regimen is altered.

Do NOT use the (red) standard SAPG 'Adult Parenteral Gentamicin (GGC): Prescribing, Administration & Monitoring Chart' to prescribe synergistic Gentamicin, this is for treatment dose gentamicin only.

4. Monitoring

- Take a blood sample for gentamicin analysis one hour after the first gentamicin bolus injection has been administered (a "peak" sample).
- Take a second blood sample for gentamicin analysis at the end of the first dosage interval (a "trough" sample, just before the next dose is due) then give the next dose. **Do NOT delay giving the second gentamicin dose while awaiting the trough**

concentration to be reported, unless there are concerns over deteriorating renal function.

- Record the exact time of all gentamicin samples on the Synergistic Gentamicin Administration and Monitoring Chart (see Appendix below). Ensure all TrakCare sample request forms are printed at the time of sample collection (so that accurate sample times are recorded on TrakCare/Clinical Portal).
- Levels should always be taken during core hours (ideally between 9am and 2pm) to allow for process
- See the table below for advice on interpreting gentamicin concentration results.
- Monitor the patient's creatinine daily and record this on the Synergistic Gentamicin Administration and Monitoring Chart (see Appendix below).
- If the prescribed dose amount/dose frequency is altered ensure this is updated and prescribed on HEPMA.

If the measured gentamicin concentration is unexpectedly HIGH or LOW

- Were dose and sample times recorded accurately?
- Was the correct and full dose administered?
- Was the sample taken from the line used to administer the drug?
- Was the sample taken at the correct time?
- Has renal function deteriorated or improved?
- Does the patient have oedema, ascites or an extreme weight?

If in doubt, take another sample before re-dosing and / or seek advice from pharmacy.

Gentamicin Result	Recommended Action
Both the peak result is in range (10-12mg/L) - AND the trough result is in range (<1mg/L)	• Continue the present dosage regimen (dose amount and dose frequency). • **There is no need to repeat the peak sample** unless there are concerns over response to therapy. • Repeat the trough sample every 2 days, provided renal function remains stable. • Repeat the trough sample daily and discuss with pharmacy if renal function changes/is unstable. • Target trough for ongoing monitoring <1mg/L.
The trough sample is ≥1 mg/L	• **See above for checks to make before interpreting the result** • **If a further dose has already been administered:** take another trough sample at the appropriate time and **await the result before re-dosing.** Seek advice from pharmacy and do NOT give a further dose until the gentamicin concentration is <1 mg/L. • **If a further dose has not already been administered**: discuss with pharmacy. • Do NOT give a further dose until the gentamicin concentration is <1 mg/L.
The peak result is out of range	• **See above for checks to make before interpreting the result** • Discuss with pharmacy.

5. Duration of Synergistic Gentamicin

Microbiology or ID should be consulted to advise on the duration of synergistic gentamicin:

- Within 24 hours of starting empirical antibiotic therapy
- At 1 week of therapy, if continuation of gentamicin is being considered at that point
- If the patient is causing concern (e.g. failure to respond, evidence of toxicity)
- 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 up to 2 weeks, except on microbiology/ID advice. The addition of synergistic gentamicin in staphylococcal **native valve** IE is no longer routinely recommended as it increases renal toxicity without evidence of additional benefit.

If a patient is switched from full treatment dose gentamicin to synergistic dosing (without a significant break in therapy) then the days of full dose gentamicin therapy **would** count towards the intended synergistic course duration.

6. 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%)
- 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 usually associated with prolonged gentamicin use (usually >7 days, however it may occur at any time) 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 above for details). Patients should be asked regularly about any signs and symptoms of ototoxicity, 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. Contact the local audiology department directly via routine referral route.
- If ototoxicity is suspected **stop** gentamicin treatment and refer to microbiology/ID for advice on ongoing therapy

7. Gentamicin Patient Information Leaflet

All patients prescribed synergistic gentamicin should be given a copy of the Gentamicin Patient Information Leaflet ‘Information for patients about intravenous gentamicin’ (see Appendix) at the earliest opportunity. If this is not possible the reasons for non-issue of the leaflet should be recorded in the patient medical notes.

Adult Parenteral Synergistic Gentamicin: Administration & Monitoring Chart

Adult Parenteral SYNERGISTIC GENTAMICIN Administration & Monitoring Chart

Not for use in renal unit, patients receiving RRT or those with a creatinine clearance <21ml/min - Refer to the full NHS Forth Valley 'Guidance on synergistic use of gentamicin' for further information

Patient name : …….. Age: …….. Sex: M / F

Date of birth : …….. Weight: …….. Height: ……

CHI no .: …….. Creatinine: …….. on: ……. /……. /……

Affix patient label

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 (the dose is based on **actual** body weight unless obese, then use **maximum** body weight – see table below). **Doses should be administered by IV bolus injection over 3 – 5 minutes.**

Weight [Use ABW (or MBW if obese – see last page)]	ONCE DAILY Dose of Gentamicin
43kg to 49kg	140mg
50kg to 56kg	160mg
57kg to 64kg	180mg
65kg to 70kg	200mg
71kg to 76kg	220mg
≥77kg	240mg

Step 2: Prescribe gentamicin on HEPMA including exact dose and frequency **ONCE DAILY.** Doses should be prescribed within core hours - synergistic gentamicin should never be given overnight.

Step 3: Administration and monitoring of gentamicin (**record all doses and levels using the chart overleaf**)
- Take a 'peak' level 1 hour after the first gentamicin bolus dose.
- Take a 'trough' level before the second gentamicin dose but DO NOT await the result before re-dosing unless there are concerns about deteriorating renal function. Thereafter take a trough level at least every 2 days or daily if unstable renal function. Levels should always be taken during core hours (ideally between 9am and 2pm) to allow for processing.
- Record the exact time of ALL gentamicin samples on the sample request form and overleaf on this chart. Contact pharmacy if uncertain on interpretation of levels.

Step 4: Assess ongoing need for gentamicin daily and any signs of toxicity – Ask patients about signs of ototoxicity regularly and check renal function daily. Refer to audiology if >7 days or signs of ototoxicity

Patient Name: …….. **CHI Number:** ……..

TOXICITY Renal & Oto-vestibular Function MUST be reviewed daily	Synergistic Gentamicin Administration Record				Synergistic Gentamicin Monitoring Record				
	Complete each time gentamicin is administered **(in addition to HEPMA)**				To be completed by ALL staff taking blood forgentamicin concentration monitoring **Record ALL sample dates/times accurately below**				
	Date given	Gentamicindose (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
EXAMPLE **Cr =70 micromol /L**	30/05/2024	180mg	08.00	Sig 1: EP | Sig 2:	31/05/24	07.55	AJ Young (Staff Nurse)	0.6mg/L	Trough Level
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:					
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:					
Cr = micromol /L				Sig 1: | Sig 2:					

Appendix 2:
Maximum Body Weight Table for Creatinine Clearance Calculation

maximum-body-weight-table.pdf (sapg.scot)

Maximum body weight table			
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

Alternative Formats

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