Intravenous Gentamicin use in Adults (Hartford, 7mg/kg)

Background

This policy covers the use of intravenous (IV) gentamicin in adults using the **Hartford dosing guidance, a higher dosing of 7mg/kg**. Evidence for this dosing regimen is provided below.

The policy is for the use of gentamicin for the treatment of infection only. SAPG recommendations on gentamicin dosing for surgical prophylaxis are provided elsewhere.

The guidance **does not apply** to gentamicin use in the following:

- synergistic treatment of endocarditis or *Staphylococcal* bone infection
- patients treated in Renal units or receiving haemodialysis or haemofiltration
- major burns
- ascites
- age < 16 years
- cystic fibrosis (refer to local guidelines), and
- pregnancy (refer to local guidelines).

Contra-indications and cautions

- Contra-indications to gentamicin therapy – hypersensitivity, myasthenia gravis.
- Cautions to gentamicin therapy:
  - Patients with decompensated liver disease - aminoglycosides are associated with an increased risk of renal failure.
  - Concurrent administration of neurotoxic and / or nephrotoxic agents increases the risk of gentamicin toxicity. Review therapy and consider amending or withholding nephrotoxic drugs during gentamicin treatment. Avoid co-administration with the following:
    - neuromuscular blockers
    - other potentially nephrotoxic (e.g. NSAIDs and ACE Inhibitors) or ototoxic drugs
    - potent diuretics, and
    - other aminoglycosides.

    This list is not exhaustive – consult the Summary of Product Characteristics (eSPC) for a full list (www.medicines.org.uk)
  - Chronic Kidney Disease (CKD) Stage 4 or more, known or suspected acute kidney injury in the previous 48 hours (≥ 50% increase in baseline serum creatinine or oliguria > 6 hours). If gentamicin is clinically indicated, give one dose as per guidance and check with microbiology or an infection specialist before giving a second dose.

Prescribing and documentation

- To improve the prescribing of gentamicin, ensure consistency and reduce risk, standardised charts (agreed nationally) should be used to document the prescription, administration and monitoring of gentamicin. These should be used for prescribing treatment doses of gentamicin in conjunction with the existing inpatient prescribing chart (e.g. kardex) and medical / nursing documentation.
- These charts contain a step-wise approach to safe and effective prescribing and key points of advice on monitoring, interpreting and re-prescribing.
- An Antimicrobial app and/or an online calculator is available in all boards and should be used to calculate the initial dose.

Reference: *Nicolau DP, Freeman CD, Belliveau PP, et al. Experience with a once-daily aminoglycoside program administered to 2,184 adult patients. Antimicrob Agents Chemother. 1995; 39: 650 – 655*

STEP 1: Calculate, prescribe and administer the first dose

- To reduce risk of mortality, commence gentamicin administration within 1 hour of recognising sepsis.
- *If creatinine is known* – use the online calculator or app (preferred method). The guidelines in Box 2 (below) can be used if the online calculator is not available. The dose amount is based on estimated creatinine clearance (Box 1) and actual body weight or a corrected dosing weight (CDW) if the patient is obese (Box 2).
- *If creatinine is not known* – give 7 mg/kg gentamicin (maximum 600 mg) or, if chronic kidney disease (CKD) 5, give 2.5 mg/kg (maximum 180 mg) on advice of senior staff. Calculate the dose using actual body weight or corrected body weight if the patient is obese.
- Give the recommended dose by infusion in 100 mL sodium chloride 0.9% over 1 hour and ensure the time of administration is noted on the medicine chart.

Box 1: Estimation of creatinine clearance (CrCl)

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

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

Cautions:

- Use actual body weight or maximum body weight, whichever is lower. For maximum body weight see https://www.sapg.scot/media/4471/maximum-body-weight-table.pdf
- In patients with low creatinine (< 60 micromol/L), use 60 micromol/L.
- Note: Use of estimated glomerular filtration rate (eGFR) is not recommended.

Box 2: Initial GENTAMICIN doses

- *If creatinine clearance is > 20 mL/min and the patient is* ***not obese***, calculate the dose by multiplying actual body weight by 7 (i.e. **7 mg/kg**) to a maximum dose of 600 mg. Round this to the nearest 40 mg for ease of administration. (see Table 1)

- *If creatinine clearance is > 20 mL/min and the patient is* ***obese*** *(actual weight is >20% above their Ideal body weight)* calculate the gentamicin dose by multiplying their **corrected dosing weight** (CDW) by 7 (i.e**. 7 mg/kg CDW**) to a maximum dose of 600 mg. Round this to the nearest 40 mg for ease of administration (see Table 1).

  CDW = ideal body weight + 0.4 (actual body weight – ideal body weight)

  For ideal body weight see https://www.sapg.scot/media/4470/ideal-body-weight-tables.pdf

  If creatinine clearance ≤ 20 mL/min, first confirm that gentamicin is the most appropriate treatment. Calculate the initial dose by multiplying the patient's actual body weight (or corrected dosing weight if the patient is obese) by 2.5 (i.e. **2.5 mg/kg**) to a maximum of 180 mg. Alternatively a **SINGLE** dose of 7 mg/kg may be considered (do not repeat this dose).

Table 1: Initial GENTAMICIN doses

Creatinine Clearance (mL/min)	Actual body weight (use corrected dosing weight if the patient is obese)								
	40-44 kg	45-49 kg	50-54 kg	55-59 kg	60-65 kg	66-71 kg	72-77 kg	78-82 kg	≥ 83 kg
≤ 20	2.5 mg/kg (max 180 mg) then take a blood sample after 24 hours								
> 20	280 mg	320 mg	360 mg	400 mg	440 mg	480 mg	520 mg	560 mg	600 mg

If actual body weight is < 40 kg and creatinine clearance is > 20 mL/minute, use a dose of 7 mg/kg and round to the nearest 20 mg.
Note that patients who have unusual clinical characteristics, such as weight < 40 kg, weight >120 kg, age >90 years may require dose adjustments and require close monitoring. Contact pharmacy for advice.

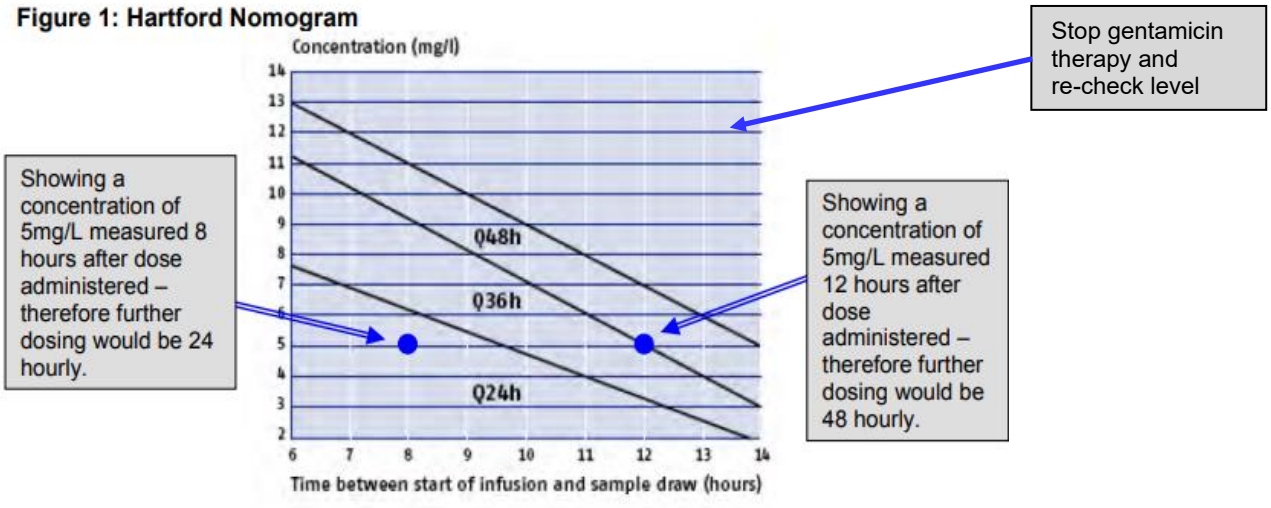
STEP 2: Monitor creatinine and gentamicin concentrations and establish the dosage regimen

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

If creatinine clearance is > 20 mL/min

- Take a blood sample 6-14 hours after the start of the first gentamicin infusion.
- Record the exact time of all gentamicin samples using the gentamicin prescribing chart AND on the sample request form.
- Record the serum concentration on the gentamicin prescribing chart.
- Plot the gentamicin concentration on the nomogram below & reassess the dose/dosing interval as indicated.
- If the result is on the line, choose the longer interval. If the level is above the 48 hourly line (Q48h), stop therapy and reassess the dosage regimen. Do not give a further dose until the concentration is <1 mg/L.

Figure 1: Hartford Nomogram



If creatinine clearance is ≤ 20 mL/min

- Take a blood sample 24 hours after the start of the gentamicin infusion.
- Record the exact time of all gentamicin samples using the gentamicin prescribing chart AND on the sample request form.
- If therapy is to continue, give a further dose once the measured concentration is < 1 mg/L.

General points

- Document the action taken in the medical notes and on the gentamicin prescribing chart.
- Undertake pre-prescribing checks (Boxes 3 & 4 on page 5) to assess the risk of renal toxicity and ototoxicity.
- Prescribe the next dose as appropriate.
- If a blood sample is not taken, is lost or is taken at wrong time ***and*** if there is any concern about patient's renal function, take a sample 20-24 hours after the start of the gentamicin infusion and wait for the result before giving the next dose. Otherwise, take a blood sample after next dose.

If the measured concentration is unexpectedly HIGH or LOW, consider the following:

- Were dose and sample times recorded accurately?
- Was the correct dose administered?
- Was the sample taken from the line used to administer the drug?
- Was the sample taken during drug administration?
- Has renal function declined or improved?
- Does the patient have oedema or ascites?

If in doubt, take another sample before re-prescribing and / or contact pharmacy for advice

STEP 3: Assess daily the ongoing need for gentamicin and signs of toxicity

- Take a further sample 6-14 hours after the dose at least every 2 days. If the concentration is unexpectedly high, or if renal function alters, daily sampling may be necessary.
- If the patient is receiving 36 or 48 hourly dosing, a level should be checked after each infusion.
- To minimise the risk of toxicity, duration of treatment should normally be limited to 72 hours. All gentamicin prescriptions that continue beyond 3-4 days of treatment must be discussed with microbiology or an infection specialist. Consider changing to an oral alternative - refer to the IV to Oral switch policy.

Box 3: Renal toxicity

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

Box 4: 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. Multiple courses of gentamicin are also a risk factor for ototoxicity.
- Stop treatment if ototoxicity is suspected and refer to microbiology or an infection specialist for advice on future therapy and refer to ENT for assessment.
- If gentamicin continues for > 7 days, consider referral to audiology for assessment.