Tobramycin Guidance for Adult Cystic Fibrosis Patients

This guideline is for adult cystic fibrosis patients only. Please do not use this guideline for other patient groups as the doses and frequency are different.

Exclusion criteria
Therapy with aminoglycoside antibiotics is not considered appropriate in patients with the following:

- acute kidney failure (>50% increase in baseline serum creatinine or oliguria >6 hours in previous 48 hours)
- chronic kidney disease (eGFR < 30ml/min/1.73m^2)
- previous serious adverse event to aminoglycoside antibiotics
- renal replacement therapy

Cautions
Renal function should be checked at baseline before starting treatment.

Senior consultation required BEFORE starting treatment in the following situations:

- Patients on other **nephrotoxic drugs** such as NSAIDs or ACE inhibitors, even if renal function is normal
    - **Post-transplant patients** taking **tacrolimus** or **ciclosporin** which are nephrotoxic; consider alternative treatment or monitor serum concentrations and renal function regularly. (NB: immunosuppressant drug concentrations should also be monitored when starting any antibiotics).

- Situations affecting **fluid balance, distribution or elimination** such as:
    - Fluctuating renal function — ensure renal function checked regularly; monitor serum concentrations regularly, review dose and consider alternative treatment.
    - Pregnancy — use alternative agent or use once daily dose to limit exposure to baby; seek advice and monitor regularly.
    - Ascites — risk of accumulation, monitor serum concentrations daily or avoid.
    - ITU admission — may require higher dose, and risk of renal impairment; check levels daily and monitor renal function.

In these situations alternative therapy should be considered. If tobramycin is required the starting dose may need to be adjusted and close monitoring of renal function and tobramycin concentrations should be carried out more frequently (up to daily). Seek advice.

Vestibular and oto-toxicity can occur at normal levels

- Patients should be warned to report any dizziness, unsteadiness on feet, tinnitus, bobbing oscillopsia (vertical bouncing of surroundings), hearing loss, nausea and vomiting.
- Toxicity is due to accumulation within the inner ear and is more likely following prolonged and repeated courses (not related to serum levels).
- Therapy should be stopped in patients showing any signs of toxicity.

1. Checklist for starting treatment

- U&Es
- Consider pregnancy test, especially if no formal contraception documented
- Arrange levels before and after 3rd dose (see below)

2. Dosage Calculation – 1st course

- Determine current **body weight** (kg) and **height** (cm)
- If BMI > 30 kg/m^2 use ideal body weight for calculation. (BMI calculator can be found here)
- Calculate **Body Surface Area** (m^2) (BSA calculator can be found here)
- Calculate dose using table below.

Table 1. Starting dose and volume calculation

BSA (m^2)	12 hourly dose	Volume (ml)
<1.15	120 mg	3.0
1.16 – 1.32	140 mg	3.5
1.33 – 1.49	160 mg	4.0
1.50 – 1.65	180 mg	4.5
1.66 – 1.82	200 mg	5.0
1.83 – 1.99	220 mg	5.5
2.00 – 2.16	240 mg	6.0
2.17 – 2.33	260 mg	6.5

Dose = 120mg/m^2 body surface area TWICE daily 12 hours apart
(round doses to nearest 20mg), given as an **IV bolus over 4-5 minutes**.

- Ideally doses are given 12 hours apart e.g. 10am and 10pm. Prescribe on HEPMA and add 'Patient Note' stating can be given as IV bolus over 4-5 minutes and when levels should be taken.

3. Dosage Calculation – subsequent courses

- Prescribe the dosage regimen that was previously identified as satisfactory for the patient. This information can obtained from:
  i. the patient's medical notes/medicine charts
  ii. previous HEPMA records
  iii. the CF team
- Recalculate dose if a significant change (e.g. >10%) in body weight or renal function has occurred since previous course.

4. Monitoring of Tobramycin Concentrations

- **Check trough and peak concentrations on the 2nd or 3rd dose.**

Trough	take immediately before a dose is given
Peak	take **EXACTLY one hour** after a **BOLUS** dose is given

- **Accurate times when doses are given and levels taken are required to work out dose changes.**

5. Review of levels and dose

- Target concentrations:

Trough	**< 1 mg/L**
Peak (after BOLUS dose)	**8 – 12 mg/L**

Results within target range (and no risk factors for accumulation - see page 1):

- continue current dose
- patients who are clinically stable, with stable renal function and no risk factors for toxicity do not require further peak levels but a trough level should be checked during the 2nd week
- consider repeating serum concentrations more often in patients with fluctuating renal function
- further levels should be checked if patient receives a 3rd week of treatment

Levels outwith range:

- **There is no need to contact a pharmacist or adjust doses out with hours**
- Refer to Adult CF pharmacist (bleep 5059) or Antimicrobial pharmacist (4732)
- A trough of >1mg/L and <2mg/L may be acceptable in some cases
- Always confirm EXACT timings of dose and samples when reviewing results out with target range
- If samples were not collected at the correct times, keep on same dose and re-check BEFORE making dose adjustments
- This is a guide only. Please seek advice if you are not sure.
- Following any dose adjustment, the peak and trough concentrations should be re-checked on the 2nd or 3rd dose.

Table 2. Dose adjustments for results out with target range

low peak	7.0 – 7.9 mg/L	Move up by one dose band (see table 1) and recheck levels.
	< 6.9 mg/L	Confirm timings and dose administered correctly. Contact pharmacist for advice. May need increased by more than one dose band.
high peak	> 12 mg/L	If trough < 1mg/L – may be able to continue with current dose if not too high, seek advice. If trough > 2mg/L - decrease dose by one dose band (see table 1) and recheck levels.
high trough	> 2 mg/L	Seek advice from pharmacist. Check renal function. Confirm dose and timings correct. Consider holding dose and decreasing dose by one dose band (see table 1) and recheck levels.
high trough	1-2 mg/L	Seek advice from pharmacist. Check renal function. Confirm dose and timings correct. May be acceptable to continue current dose and recheck levels.