

## **AMINOGLYCOSIDE GUIDELINE**

## **GENTAMICIN, AMIKACIN, TOBRAMYCIN**

This guideline does <u>NOT</u> cover:

- Dosing and monitoring for Cystic Fibrosis.
- Antibiotic indications or intravenous method of administration of medication.

See the relevant guidelines via the Trust intranet DMS

Aminoglycosides are nephrotoxic – caution alongside concomitant nephrotoxic drugs – see page 6

# AMINOGLYCOSIDES SHOULD BE AVOIDED WHEREVER POSSIBLE IN MYASTHENIA GRAVIS Please see Alder Hey guidance

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## **TERMS and ABBREVIATIONS:**

| CGA: Corrected Gestational Age  |
|---|
| = gestational age + chronological age   |
| AdjBW: Adjusted Body Weight (kg)  |
| = 0.35*(total body weight (kg) – ideal body weight (kg)) + ideal body weight (kg)                           |
| IBW: Ideal Body Weight (kg)   |
| Can be determined by measuring height and using that to identify height centile for their age using         |
| iGrow. Their IBW is then selected according to their weight at the same centile as their height in age.     |
| eGFR (estimated glomerular filtration rate) – <u>using Modified Bedside Swartz as specified in the BNFc</u> |
| Child > 1 month: eGFR (ml/min/1.73m <sup>2</sup> ) = 35 x height(cm) / serum creatinine(µmol/L)             |
| Child $\leq 1$ month: eGFR (ml/min/1.73m <sup>2</sup> ) = 30 x height(cm) / serum creatinine( $\mu$ mol/L)  |



## THERAPEUTIC DRUG LEVEL MONITORING:

Therapeutic drug monitoring is the process of measuring the levels of medication in the blood. It is important for two reasons:

- To ensure doses are therapeutic and treating infections low doses increase the risk of resistance.
  - To ensure doses are not toxic to patients high doses increase the risk of side effects

**Pre-dose** levels measure the lowest concentration of drug in the bloodstream shortly before another dose is given.

- For 24-36 hourly dosing: pre-dose levels should be taken within 2 3 hours before the next dose is due.
- For endocarditis (8 hourly dosing): pre-dose levels should be taken 1 hour before the next dose is due.

**Post-dose** levels measure the highest concentration of drug in the bloodstream shortly after a dose is given. To be taken 1 hour after commencing administration of a dose.

Levels may be taken at other times on advice from a Pharmacist.

Patients on Critical Care may be managed differently based on their clinical status. Critically ill children can have multiple organ dysfunction, and the common use of renal replacement therapy and ECMO can significantly alter how critically ill children manage aminoglycosides. They are also more likely to present with severe infection, requiring more frequent dosing of aminoglycosides or amendments to target pre-dose and post-dose levels. As a result, they may require more frequent monitoring of levels and U&Es to ensure therapeutic levels and maintaining safety.

## **MULTIDISCIPLINARY ROLES AND RESPONSIBILITIES:**

All members of the multidisciplinary team are responsible for the safe and effective delivery of medication to patients, and appropriate handover to other members of the MDT.

| Prescriber<br>responsibilities | Choosing the correct and safe choice of antimicrobial drug;<br>Prescribing the initial dose;<br>Ordering the initial serum level;<br>Monitoring kidney function;<br>Acting upon reported levels in good time;<br>Prescribing dose changes in response to level results after taking advice from a Pharmacist;<br>Ensuring the duration of treatment is appropriate. |
|--------------------------------|---|
| Nurse<br>responsibilities      | Be aware of all aminoglycoside prescriptions for patients under their care<br>Taking blood samples at correct times;<br>Checking dosing is correct and safe;<br>Administering doses at correct times;<br>Monitoring fluid balance;<br>Acting upon reported levels in good time.   |
| Pharmacist<br>responsibilities | Be aware of all aminoglycoside prescriptions for patients under their care;<br>Checking dosing is correct and safe;<br>Ensuring serum levels are scheduled to be taken at the correct times;<br>Ensuring follow up plans are documented;<br>Advising dose changes to be prescribed if level results are out of the intended target range.                           |



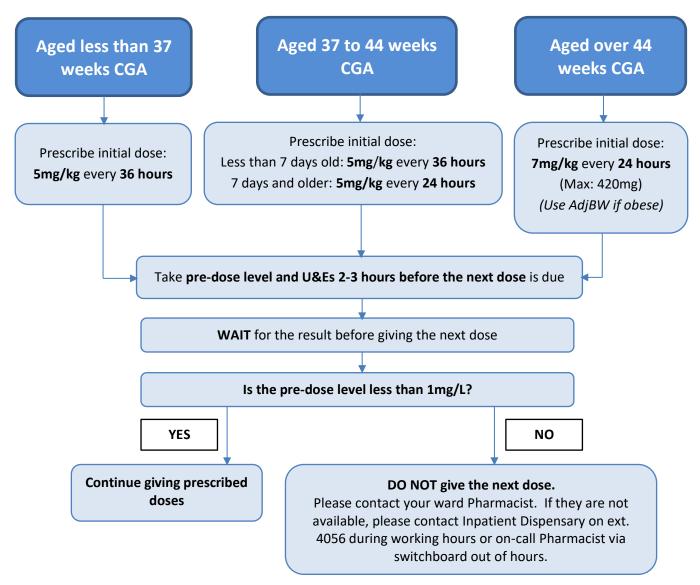
## INITIAL DOSING AND SERUM LEVEL MONITORING - QUICK REFERENCE FLOWCHARTS:

## GENTAMICIN

Flowchart for initial dosing and serum level monitoring for patients with NORMAL RENAL FUNCTION For administration details refer to the Paediatric Injectable Therapy Guidelines

See page 6 for further monitoring

Alder Hey dosing and monitoring is deliberately different to the BNFc and NICE guidance



Post-dose levels should be considered in selected babies, such as in those with:

- Oedema
- Macrosomia (birthweight more than 4.5kg) •
- An unsatisfactory response to treatment
- Proven Gram-negative infection

Advice will be provided by Pharmacy if a post-dose level is required.

IF TREATING ENDOCARDITIS, MULTIPLE DAILY DOSING IS REQUIRED - See page 10 for separate flowchart



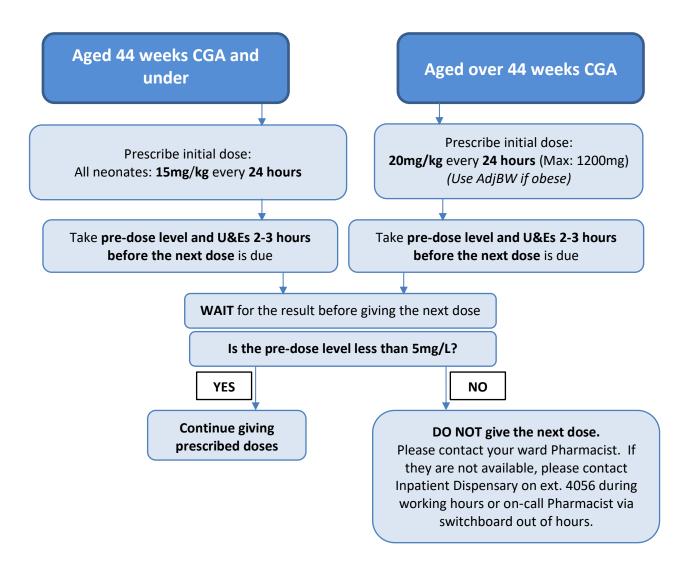
## AMIKACIN

Flowchart for initial dosing and serum level monitoring for patients with NORMAL RENAL FUNCTION

For administration details refer to the Paediatric Injectable Therapy Guidelines

See page 6 for further monitoring

Alder Hey dosing is deliberately different to the BNFc





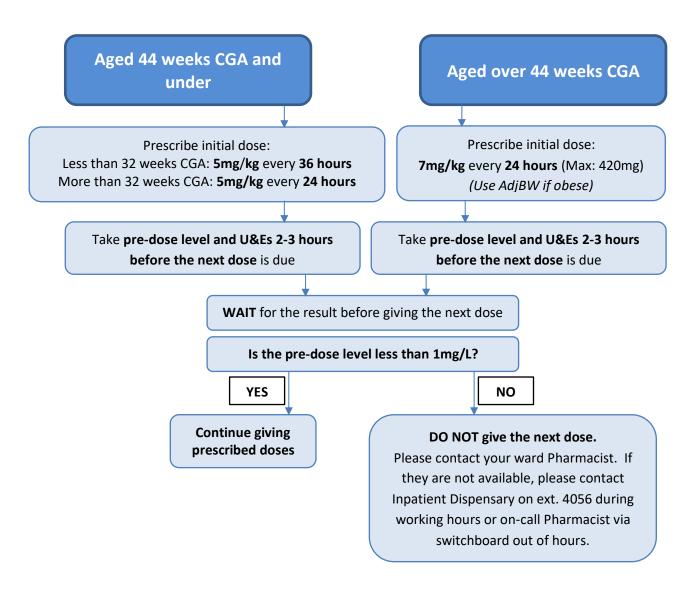
## TOBRAMYCIN

Flowchart for initial dosing and serum level monitoring for patients with NORMAL RENAL FUNCTION

For administration details refer to the Paediatric Injectable Therapy Guidelines

See page 6 for further monitoring

Alder Hey dosing is deliberately different to the BNFc





## FREQUENCY OF MONITORING FOR ALL AMINOGLYCOSIDES

#### All patients receiving aminoglycosides should have:

- Daily monitoring of renal function including: U&Es and fluid balance
- Pre-dose levels before the 2<sup>nd</sup> & 4<sup>th</sup> dose then at least every 3 doses
  - More frequent levels may be needed on the advice of a Pharmacist

#### Discuss with Nephrology team in the following situations:

- 50% rise in serum creatinine (Acute Kidney Injury (AKI) Stage 1) even if creatinine level is still within normal limits
- In patients with an AKI alert please follow Trust <u>AKI guidance</u>
- Oliguria (urine output less than 1ml/kg/hr)

#### Daily monitoring of aminoglycoside levels is recommended in the following situations:

- All patients with renal impairment (eGFR < 90ml/min/1.73m<sup>2</sup>)
- 25% rise in serum creatinine (at risk of Acute Kidney Injury) even if creatinine level is still within normal limits

#### Daily monitoring of aminoglycoside levels should be considered in the following situations:

- Patients prescribed an aminoglycoside alongside at least 1 other drug that can cause nephrotoxicity. See *Table 1 below*.
- Signs of intravascular compromise (including poor cardiac output)
- Dehydration (including due to diarrhoea / vomiting)

#### Table 1: Drugs that can cause nephrotoxicity (this list is not exhaustive)

| <b></b>            |                         |                |                |
|--------------------|-------------------------|----------------|----------------|
|                    | Cephalosporins          |                | Amphotericin   |
|                    | Pentamidine             |                | Aciclovir      |
| Antibiotics        | Piperacillin/tazobactam | Antifungals /  | Cidofovir      |
| Antibiotics        | Teicoplanin             | Antivirals     | Ganciclovir    |
|                    | Trimethoprim            |                | Valaciclovir   |
|                    | Vancomycin              |                | Valganciclovir |
|                    | Chlorothiazide          |                | Cantonril      |
| Diuretics          | Furosemide              | ACE Inhibitors | Captopril      |
|                    | Spironolactone          |                | Lisinopril     |
|                    | Celecoxib               |                | Carboplatin    |
|                    |                         |                | Cisplatin      |
| Analgesics         | Parecoxib               | Cytotoxics     | Ifosfamide     |
| Ū                  | Ibuprofen               | •              | Melphalan      |
|                    | Diclofenac              |                | Methotrexate   |
|                    | Ciclosporin             |                |                |
| Immunosuppressants | Tacrolimus              |                |                |



## PRE-EXISTING RENAL IMPAIRMENT (eGFR < 90ml/min/1.73m<sup>2</sup>):

#### <u>See page 1 for eGFR formula</u>

- For patients with a background of chronic kidney disease (CKD), aminoglycosides should be initiated with advice from the Infectious Diseases/Microbiology (ID/Micro) or Renal team.
- In neonates, if it is considered from pre-natal investigations that there is potential for renal impairment AVOID aminoglycoside use and consult ID/Micro and Renal teams.

## **\*\*CHECK PRE-DOSE LEVEL BEFORE GIVING EVERY DOSE\*\***

#### **Dosing and Monitoring:**

#### For patients with renal impairment NOT on any form of dialysis:

Gentamicin:Follow flowchart on page 8Amikacin:Follow flowchart on page 9Tobramycin:Rarely indicated in renal impairment. Contact Pharmacy for dosing and monitoring advice.

#### For patients on Haemodialysis:

See the Renal Replacement Central Venous Catheter Infection Prevention and Control Guidance

#### For patients on other forms of dialysis (CVVH, peritoneal dialysis):

If pre-existing renal impairment or AKI follow relevant flowchart for eGFR < 20ml/min/1.73m<sup>2</sup> If no renal impairment suspected follow relevant flowchart for eGFR > 20ml/min/1.73m<sup>2</sup>

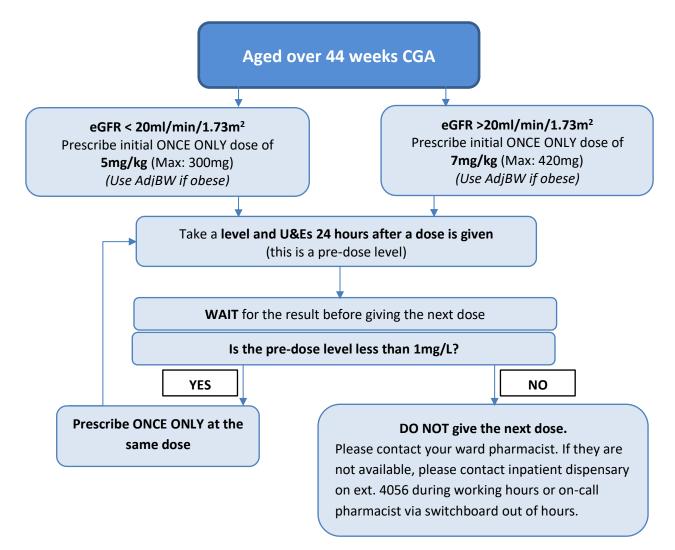


## **GENTAMICIN – PRE-EXISTING RENAL IMPAIRMENT**

#### For Neonates, 44 weeks CGA and under, with pre-existing renal impairment, discuss with ID/Micro and Renal

#### teams. If approved for use, discuss dosing with Pharmacy.

For administration details refer to the <u>Paediatric Injectable Therapy Guidelines</u>



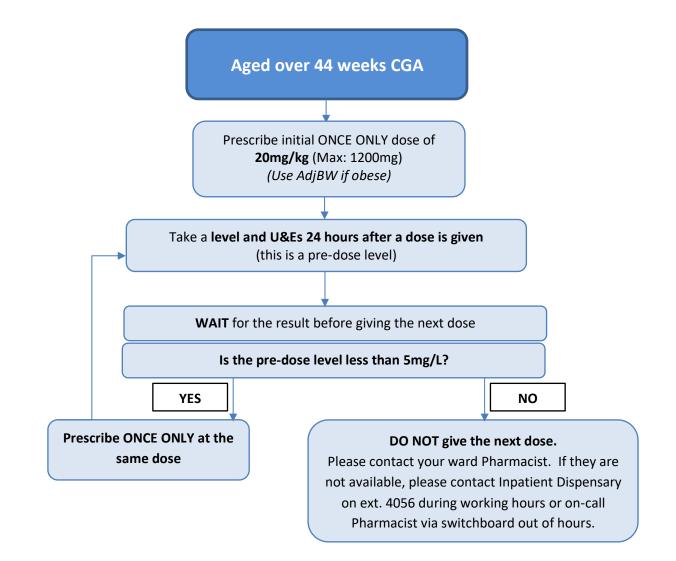


## **AMIKACIN – PRE-EXISTING RENAL IMPAIRMENT**

#### For Neonates, 44 weeks CGA and under, with pre-existing renal impairment, discuss with ID/Micro and Renal

#### teams. If approved for use, discuss dosing with Pharmacy.

For administration details refer to the Paediatric Injectable Therapy Guidelines

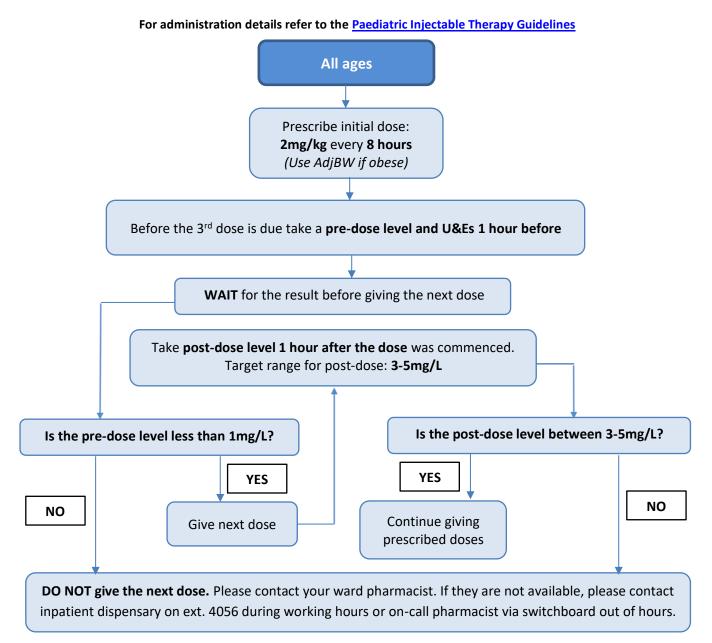




## **ENDOCARDITIS – FLOWCHART FOR MULTIPLE DAILY DOSING OF GENTAMICIN**

The following information is for patients using gentamicin for synergy alongside another medicine such as flucloxacillin. When treating gram-negative infections, the ID/Micro team may suggest using treatment dosing. Therefore, refer to appropriate treatment flowcharts above.

For more information please refer to the <u>American Heart Association guidelines</u>. Note that doses differ to BNFc doses and are taken from the guidelines above.



Further levels should be taken on the advice of a Pharmacist. Levels should be taken at least every 3 days.

Target ranges for post-dose levels may change (e.g. 5-10mg/L) depending on isolates. Pharmacy and ID/Micro will advise if target ranges need to change.



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American Heart Association, 2015. *Infective Endocarditis in Childhood: A scientific statement from the American Heart Association*. www.ahajournals.org/doi/10.1161/cir.0000000000000298

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Floto RA, Olivier KN, Saiman L, et al. US Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus recommendations for the management of non-tuberculous mycobacteria in individuals with cystic fibrosis. Thorax 2016; 71:i1-i22.

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## **APPENDIX 1: BIOCHEMISTRY AMINOGLYCOSIDE REFERENCE RANGES**

|                           | Low<br>Abnormal | Normal | High<br>Critical | Units | Auto Comment<br>for results | Guidance for Biochemistry  |
|---------------------------|-----------------|--------|------------------|-------|-----------------------------|--|
| GENTAMICIN                |                 |        |                  |       |                             |  |
| PRE-DOSE                  |                 | 0-0.9  | >=1.0            | mg/L  | >=1.0                       | Use if level is taken 0-3 hours before next dose is due<br>(21-24 hours after last dose for once daily dosing,<br>33-36 hours after last dose in neonates <7 days old,<br>5-8 hours after last dose in Endocarditis) |
| POST-DOSE                 | <5              | 5-10   | >=10.1           | mg/L  | <5 or >=10.1                | Use if level is taken 0-2 hours after the last dose is given   |
| POST-DOSE<br>ENDOCARDITIS | <3              | 3-5    | >=5.1            | mg/L  | <3 or >=5.1                 | Use if level is taken 0-2 hours after the last dose is given<br>AND<br>Patient is identified on request form as having Endocarditis  |
| RANDOM                    |                 | 0-0.9  | >=1.0            | mg/L  | >=1.0                       | Use if level is taken at any other timepoint   |
| TOBRAMYCIN                |                 |        |                  |       |                             |  |
| EXTERNAL<br>SAMPLE        |                 | -      |                  | mg/L  |                             | Use for non-Alder Hey samples  |
| PRE-DOSE                  |                 | 0-0.9  | >=1.0            | mg/L  | >=1.0                       | <b>Use if level is taken 0-3 hours before next dose is due</b><br>(21-24 hours after last dose for once daily dosing)  |
| RANDOM                    |                 | 0-0.9  | >=1.0            | mg/L  | >=1.0                       | Use if level is taken at any other timepoint   |
| AMIKACIN                  |                 |        |                  |       |                             |  |
| EXTERNAL<br>SAMPLE        |                 | -      |                  | mg/L  |                             | Use for non-Alder Hey samples  |
| PRE-DOSE                  |                 | 0-4.9  | >=5.0            | mg/L  | >=5.0                       | <b>Use if level is taken 0-3 hours before next dose is due</b><br>(21-24 hours after last dose for once daily dosing)  |
| POST-DOSE                 | <20             | 20-30  | >=30.1           | mg/L  | >=30.1                      | Use if level is taken 0-2 hours after the last dose is given   |
| RANDOM                    |                 | 0-4.9  | >=5.0            | mg/L  | >=5.0                       | Use if level is taken at any other timepoint   |



| Aminoglycoside Guideline   |   |  |  |  |
|----------------------------|---|--|--|--|
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| Name of originator/author: | Samiah Awan, Georgina McIntosh, Stephen McWilliam and                     |  |  |  |
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| Approved by:               | Aminoglycoside Working Group – March 2022                                 |  |  |  |
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