Amikacin

General Information

- Amikacin is an aminoglycoside antibiotic and has a narrow therapeutic index.
- Both **weight based dosing** and **therapeutic drug monitoring** (TDM) are essential to ensure therapeutic efficacy and to minimise the risk of adverse effects such as nephrotoxicity, vestibular and ototoxicity.
- **Standard Once Daily regimen** is recommended for the treatment of sepsis and most other infections.
- These recommendations do not apply to the use of amikacin in endocarditis, cystic fibrosis, pregnancy, renal replacement therapy, or those on multiple daily dosing schedules.
- Use dose calculations as recommended below, however **do not delay 1 st doses** in patients requiring urgent therapy if renal function information is not available.
- A **stat or single dose** if often sufficient.
- Review need for ongoing treatment with amikacin on a daily basis . Treatment courses extending beyond **3-5 days** are rarely required and are associated with an increased risk of adverse effects.
- A maximum total adult dose of 15 g (i.e. entire treatment course) should not be exceeded.
- Please discuss patients on prolonged courses of amikacin with the clinical microbiology team.

Adverse Effects

- **Vestibular and ototoxicity** can occur independently of serum amikacin levels and duration of treatment however the risk increases significantly with higher cumulative doses and courses of longer durations.
- **Nephrotoxicity** : Consider renal function, volume status, and the use of concomitant nephrotoxic agents such as NSAIDs, ACE inhibitors, and diuretics, when prescribing aminoglycosides.

Cautions and Contraindications

- Amikacin is a restricted antimicrobial and should only be prescribed for the treatment of infections due to gentamicin resistant Gram negative bacilli or if recommended by a consultant microbiologist
- Consider renal function, hydration status and concomitant nephrotoxic medicines
- Therapeutic Drug Monitoring is necessary to prevent toxicity notably nephrotoxicity & ototoxicity.
- Risk of ototoxicity increases with higher cumulative doses and longer treatment courses.
- Caution advised in patients with auditory and vestibular disorders, and conditions characterised by muscular weakness.
- Aminoglycosides (Gentamicin, Amikacin, Tobramycin) are contraindicated in patients with **myasthenia gravis** as they may impair neuromuscular transmission in these patients

Dose Calculations

Step 1: Weigh patient (kg) to determine **Actual Body Weight** and record height.

Step 2: Calculate the **Body Mass Index** and/or **Ideal Body Weight** to determine if the patient is obese. (Please see formulae for weight calculation)

Step 3 : **Obese Dosing Weight/Adjusted Body Weight** should be used in CrCl and dose calculations if **BMI >30 kg/m ^{2}** or if ABW is 20% more than Ideal Body Weight. (Please see formula for weight calculation)

Step 4: Calculate **Creatinine clearance** using **Cockcroft-Gault equation** using either **Actual Body Weight or Obese Dosing Weight/Adjusted Body Weight** as indicated above. Use of Cockcroft Gault formula is less reliable in children, acute renal failure, oedematous states, muscle wasting, amputees, and malnourished patients.

(Please see MdCalc Creatinine Clearance Calculator)

Step 5: Calculate the **amikacin dose** to be administered based on CrCl and weight (use Obese Dosing Weight/Adjusted Body Weight if obese) as per the table below.

Creatinine Clearance	Dose
> 50 ml/min	15 mg/kg q24h (max 1.5g)
21-50 ml/min	10 mg/kg q24h (max 1.5g)
10-20 ml/min	4 mg/kg stat. Redose when level <5 mcg/ml.
<10 ml/min	2 mg/kg stat. Redose when level <5 mcg/ml.
Dialysis	Seek specialist advice.

Monitoring and Levels

- Order serum trough level to be taken 16-24h after the first dose has been given.
- Amikacin trough (pre-dose) level for once-daily dosing should be ≤**5 mcg/ml.**
- Ensure laboratory request form and serum sample is labelled with **sample time and date** . Ensure the timing of the last dose is accurately recorded.
- Monitor renal function.
- **Check and interpret trough level** result, renal function AND review need for continued treatment prior to prescribing subsequent doses. **NB.** Doses should never be held whilst awaiting trough levels in patients with sepsis or severe infection.
- These recommendations do not apply to TDM and target trough levels for patients on a multiple daily dosing schedules. Discuss these patients with pharmacy and/or clinical microbiology.

Trough level	Action
≤ 5mcg/ml	Review need for further dose. Administer same dose again if ongoing aminoglycoside treatment indicated and renal function is stable.
> 5mcg/ml (High)	Ensure level was taken >16h post dose. Recheck level and redose if required when level ≤5mcg/ml. May need to extend dosing interval and/or reduce dose if ongoing treatment required- discuss with Microbiology/Pharmacy.

References

1. Renal Drug Database. www.renaldrugdatabse.com . 9th September 2019.
2. BNF. https://doi.org/10.18578/BNF.716968910 . 12 th August 2020.

Amikacin Dosing Algorithm

Amikacin

1. SELECT PATIENT APPROPRIATELY

For EMPIRIC therapy (pathogen not known) use AMIKACIN instead of Gentamicin in patients with:

- A history of gentamicin resistant Gram negative pathogens (review previous microbiology test results).
- Sepsis requiring ICU review/admission, or septic shock.
- Sepsis when using concurrent ciprofloxacin in patients with IgE-mediated allergy/anaphylaxis to or severe reaction to penicillin (due to risk of co-resistance).

Contraindications: Myasthenia gravis.

2. PRESCRIBE DOSE

Max. amikacin dose = **1.5g** daily

Use Obese Dosing Weight (ODW) if BMI > 30kg/m^2 or if ABW is 20% more than IBW.

In oliuria (urine output < 500ml/day), dose as per CrCl < 10ml/min.

Creatinine Clearance	Dose
>50 ml/min	15 mg/kg q24h
21-50 ml/min	10 mg/kg q24h
10-20 ml/min	4 mg/kg stat. Redose based on level.
<10 ml/min	2 mg/kg stat. Redose based on level.
Dialysis	Seek specialist advice.

BMI = Weight (kg) / Height^2(m^2)

ODW = IBW + 0.4 (Actual weight – IBW)

IBW = R + (2.3kg for every inch over 5ft)

R = 50 for males and 45.5 for females

CrCl = $\frac{n \times (140 - age) \times weight\ (kg)(ODW\ if\ obese)}{Serum\ Creatinine\ (\mu mol/l)}$

n = 1.23 for males and 1.045 for females

IBW = Ideal Body Weight

ODW = Obese Dosing Weight

3. ORDER A TROUGH LEVEL TO BE TAKEN 16-24H AFTER THE FIRST DOSE

> Ensure request form and serum sample are labelled with 1) Date & time of the last dose and 2) Date & time level was taken.

> Monitor renal function.

4. CHECK AND INTERPRET TROUGH LEVEL RESULT

Trough level	Action
≤ 5mcg/ml	Review need for further doses. Administer same dose again if ongoing aminoglycoside treatment indicated and renal function is stable.
> 5mcg/ml *(high)*	Ensure level was taken >16h post dose. Recheck level and redose if required when level ≤5mcg/ml. May need to extend dosing interval and/or reduce dose for subsequent doses depending on the creatinine clearance - discuss with Clinical Microbiology/Pharmacy.