

Guidelines on the use of ‘extended interval’ gentamicin therapy

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

Introduction

This guideline covers the prescribing and monitoring of gentamicin for all patients (except paediatrics and neonates) prescribed gentamicin (there are exclusions listed within the guidance).

This guideline is for use by the following staff groups:

All qualified healthcare professionals involved in prescribing, administering or monitoring gentamicin.

Lead Clinician(s)

Elisha Zafar Specialist Pharmacist for Infectious Diseases and Deputy Lead for Antimicrobial Stewardship

Antimicrobial Stewardship Group on: 24th August 2023

Approved by Medicines Safety Committee on: 13th September 2023

Review Date: 13th September 2026

This is the most current document and is to be used until a revised version is available

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It is the responsibility of every individual to check that this is the latest version/copy of this document.

Key amendments to this Document:

Date	Amendment	By:
11.05.06	Approved by Clinical Effectiveness Committee	
July 2010	Change of dosing regimen for gentamicin to 5 mg/kg and switch to use of Urban and Craig nomogram for monitoring levels	See list
September 2010	Approved by Medicines Safety Committee	
July 2012	Reviewed –Change in author job title	K Hinton
July 2014	Document extended for 3 months	Dr Catterall
November 2014	Document extended for 1 month	Dr Catterall
June 2015	Document extended for 6 months whilst it is in the review process	Dr Catterall
November 2015	Document extended for 12 months as per TMC paper approved on 22 nd July 2015	TMC
Oct 16	Further extension as per TMC paper approved on 22 nd July 2015	TMC
November 2017	Document extended for three months whilst document under review	TLG
December 2017	Sentence added in at the request of the Coroner	
December 2017	Document extended for 3 months as per TLG recommendation	TLG
March 2018	Document extended for 3 months as approved by TLG	TLG
June 2018	Document extended for 3 months as per TLG recommendation	TLG
February 2021	Document extended as per Trust agreement 11.02.2021	
August 2021	Document extended until the end of December while alternative treatment regime is being considered and lead pharmacist AMS is in post	T Carruthers/ H Morton
December 2021	Document extended until 30/06/2022.	Approved by: MSC (CMO Chair)
July 2022	Exclusions and dosing weight (i.e. IBW for all patients) updated. Clarification on dosing and monitoring for 3mg/kg ONCE daily dosing regimens	Approved by: MSC (CMO Chair)
June 2023	Dosing changed to 5mg/kg ONCE daily for all indications except endocarditis. Dosing based on adjusted body weight. Monitoring changed to pre-dose levels for all patients.	Elisha Zafar Keith Hinton

Guidelines on 'Extended Interval' Gentamicin Regime

Introduction

Gentamicin is an aminoglycoside antibiotic which is bactericidal and active against some Gram-positive and many Gram-negative organisms. It is not absorbed from the gut and must therefore be given by injection for systemic infections. Gentamicin is potentially toxic, so serum monitoring is important to avoid both excessive and sub-therapeutic concentrations, thus preventing toxicity and ensuring efficacy. Traditionally gentamicin has been administered two to three times a day, but the 'extended interval' (EI) regimen described in this guideline has been shown to be safe, effective and more convenient (although some indications are excluded due to insufficient evidence, see below).

Aminoglycoside therapy – Gentamicin (BNF section 5.1.4)

- Broad spectrum agent
- Good Gram-negative activity
- Nephrotoxic and ototoxic
- Synergy with β -lactams
- Amikacin and tobramycin should be reserved for specific indications (e.g. cystic fibrosis and on microbiology advice)
- May be given by multiple or single daily dose

Giving gentamicin as a single large dose, rather than using the traditional two or three times per day regimes, offers several definite advantages.

These include:

- Reduced staff time in preparing and administering the drug
- Reduced drug wastage
- Timing of dose less critical (as giving the dose an hour or two early or late makes much less difference to potential toxicity than with a multiple daily dose regime)
- Dose more likely to be optimal according to pharmacodynamic principles
- Reduced staff time in taking blood for levels
- Reduced laboratory costs in measuring levels
- Once daily administration is at least as safe as multiple daily dose regimens

Exclusions to this regime

- Renal impairment (CrCl <40ml/minute using the Cockcroft-Gault equations) if necessary, discuss with clinical pharmacist or microbiologist.
- Treatment of endocarditis (use 3mg/kg ONCE daily regimen – based on ideal bodyweight) – see below
- Pregnancy
- Ascites
- Major burns (>20%)
- Amputees
- Cystic fibrosis
- Neonates

Procedure for dosing, monitoring and administering ‘Extended Interval’ Gentamicin

Dosing of Gentamicin

- The standard **treatment** dose is **5mg/kg**
- No single dose of Gentamicin should exceed 560mg
- Doses should be rounded to the nearest 40mg
- Doses of 5mg/kg or more should be given over 60 minutes to diminish the theoretical risk of a rapid rise in serum concentrations that might precipitate neuromuscular blockade

There are two options for calculating the gentamicin dose:

OPTION 1: Using the calculator in MicroGuide (preferred)

Obtain weight, height and serum creatinine for your patient (together with their age and sex).

The calculator will check if the renal function is suitable for extended interval gentamicin and inform you of the recommended dose.

A link for the calculator can be found here:

<http://wwrpharmiis01.whits.local/calculators/gentamicinCalculator.asp>

OPTION 2: Using the dosing tables below (use only if IT failure prevents calculator access)

Step 1: Calculate the ideal body weight, using the formula below, to be used in calculating the **creatinine clearance only**. This is to ensure sufficient renal function for ‘EI’ gentamicin.

Calculating IDEAL body weight	
Calculate ideal body weight (IBW) which can be calculated by:	
Men (IBW):	50kg + (2.3kg x number of inches over 5foot)
Women (IBW):	45.5kg + (2.3kg x number of inches over 5foot)
For patient’s < 5foot, use IBW = 45.5kg (women) or 50kg (men)	
* For underweight patients (i.e. their actual bodyweight is lower than their ideal bodyweight), calculate creatinine clearance according to actual bodyweight.	

Step 2: Calculate creatinine clearance.

The patient’s creatinine clearance must be >40ml/min to use ‘EI’ Gentamicin.*

For adults, calculate the creatinine clearance using the Cockcroft-Gault equations shown below. Alternatively, use the calculator on the trust intranet (under Departments A to Z, Pharmacy, Useful Resources & Weblinks, Creatinine Clearance Calculator).

Men: $CrCl = 1.23 \times \frac{(140 - \text{age}) \times \text{weight (kg)}}{\text{Serum creatinine}}$

Women: $CrCl = 1.04 \times \frac{(140 - \text{age}) \times \text{weight (kg)}}{\text{Serum creatinine}}$

*If there is renal impairment (i.e. CrCl < 40mL/min), where the Trust antimicrobial guidelines recommend gentamicin, give a **single dose** of 5mg/kg based on ideal bodyweight. On balance, the benefits of a single dose of gentamicin, in the context of sepsis and renal impairment, are likely to be greater than the harms posed from nephrotoxicity, given gentamicin's rapid bactericidal activity and low rates of resistance observed.

Step 3: Use dosing tables below. [Figure 1](#) (for all male patients) and [figure 2](#) (for all female patients) below give suggested doses of Gentamicin **5mg/kg** according to height and actual body weight and take into account a correction factor for obese patients.

Gentamicin 5mg/kg dosing tables according to height and actual body weight

MALE PATIENTS

Figure 1

MALE																														
Height																														
6'5	240	240	280	320	320	360	360	400	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560	560	560	560	560	560	560	
6'4	240	240	280	320	320	360	360	400	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560	560	560	560	560	560	560	560
6'3	240	240	280	320	320	360	360	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560	560	560	560	560	560	560
6'2	240	240	280	320	320	360	360	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560	560	560	560	560	560
6'1	240	240	280	320	320	360	360	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560	560	560	560	560
6'0	240	240	280	320	320	360	360	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560	560	560	560	560
5'11	240	240	280	320	320	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560	560	560	560
5'10	240	240	280	320	320	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560	560	560
5'9	240	240	280	320	320	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560	560	560
5'8	240	240	280	320	320	360	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560	560
5'7	240	240	280	320	320	320	360	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560
5'6	240	240	280	320	320	320	360	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560
5'5	240	240	280	320	320	320	320	360	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560
5'4	240	240	280	280	320	320	320	320	360	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560
5'3	240	240	280	280	320	320	320	320	360	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560
5'2	240	240	280	280	280	320	320	320	320	360	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	520
5'1	240	240	280	280	280	280	320	320	320	320	360	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520
5 foot and under	240	240	280	280	280	280	320	320	320	320	360	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520
Weight	45	50	55	60	65	70	75	80	85	90	95	100	105	110	115	120	125	130	135	140	145	150	155	160	165	170	175	180	185	

FEMALE PATIENTS

Figure 2

FEMALE																														
Height																														
6'5	240	240	280	320	320	360	360	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560	560	560	560	560	560	560
6'4	240	240	280	320	320	360	360	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560	560	560	560	560	560
6'3	240	240	280	320	320	360	360	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560	560	560	560	560	560
6'2	240	240	280	320	320	360	360	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560	560	560	560	560
6'1	240	240	280	320	320	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560	560	560	560
6'0	240	240	280	320	320	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560	560	560
5'11	240	240	280	320	320	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560	560	560
5'10	240	240	280	320	320	360	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560	560
5'9	240	240	280	320	320	320	360	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560
5'8	240	240	280	320	320	320	360	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560	560
5'7	240	240	280	320	320	320	320	360	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560	560
5'6	240	240	280	280	320	320	320	320	360	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560
5'5	240	240	280	280	320	320	320	320	360	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560	560
5'4	240	240	280	280	280	320	320	320	320	360	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520	560
5'3	240	240	280	280	280	280	320	320	320	320	360	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520
5'2	240	240	280	280	280	280	320	320	320	320	360	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520	520
5'1	240	240	240	280	280	280	280	320	320	320	320	360	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520	520
5'0 and under	240	240	240	240	280	280	280	280	320	320	320	320	360	360	360	360	400	400	400	400	440	440	440	440	480	480	480	480	520	520
Weight	45	50	55	60	65	70	75	80	85	90	95	100	105	110	115	120	125	130	135	140	145	150	155	160	165	170	175	180	185	

Administration and Monitoring of Gentamicin

Dosing regimen	Administration	Monitoring	Interpretation of levels	Further levels
<p>5mg/kg ONCE a day</p> <p>(Maximum dose of 560mg)</p>	<p>Dilute dose in 100ml sodium chloride 0.9% and give over 60 minutes.</p>	<p>Pre-dose level (within 0-4 hours pre-dose)</p>	<p>If level \leq 1.0mg/L, safe to continue.</p> <p>If the level is $>$1 mg/L withhold dose and recheck level after 12 hours. Alter frequency according to new dosing interval.</p>	<p>Renal function stable = twice per week level</p> <p>Renal function poor/deteriorates/AKI alert = once a day level until stable/off treatment (see below: renal monitoring)</p>
<p>3mg/kg ONCE a day</p> <p>Endocarditis patients (on microbiology advice only)</p>				
<p>Do not give more than one dose in 24 hours unless on the specific recommendation of a microbiologist or clinical pharmacist.</p> <p>Continue to give further doses of gentamicin as prescribed until the level is known, unless there are concerns regarding renal function e.g. reduced urine output or raised serum creatinine, then hold the dose until plasma level \leq 1.0mg/L</p> <p>Aminoglycoside therapy should be reviewed after three days and continuation of therapy discussed with a consultant microbiologist if prolonged therapy is considered necessary.</p>				

Procedure for obtaining gentamicin level

Ensure request form for gentamicin level printed off at the time of obtaining the level.

- Request 'Gentamicin' from ICE search bar
- Information required on the request form:
 - Patient details,
 - Drug given, dose and dosage interval
 - Date and time of last dose given
 - Time blood sample taken (trough or peak or 'EI')
- Take a 5 ml blood sample in a gold-topped Vacutainer tube between 0 to 4 hours **before** the start of the next infusion.

Further level interpretation

If the measured concentration is unexpectedly HIGH, then consider the following:

- Were the 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? *
- Was the sample accidentally or unintentionally taken post-dose? *
- Has renal function declined or improved?
- Does the patient have oedema or ascites?

* If any of these apply, repeat the pre-dose gentamicin level prior to the next dose to clarify. In patients with sudden decline in renal function, consider holding a dose or seek advice.

Renal monitoring

Daily U&E monitoring and fluid balance for all patients whilst on gentamicin

To detect Acute Kidney Injury, look for:

- An unexpected creatinine rise: daily gentamicin level
- Check for lab alert for 'acute kidney injury' (type in search box): If AKI alert stage 1-3, stop gentamicin if patient improving; otherwise discuss urgently with duty microbiologist and renal (wah-tr.referral-renal@nhs.net).

Patients at enhanced risk of gentamicin-induced ototoxicity

About 0.2% of the population carry a mitochondrial gene mutation (m.1555A>G) which increases the risk of aminoglycoside-induced ototoxicity. There have been reported cases of deafness in m.1555A>G patients with limited exposure to aminoglycosides and acceptable serum concentrations. Some cases were associated with a maternal history of deafness or mitochondrial mutations or both.

Recommendations

Colleagues are asked to:

- Check if patients have a known mitochondrial mutation or a family history of ototoxicity before prescribing an aminoglycoside
- Consider the need for genetic testing, in those patients requiring recurrent or long-term treatment with aminoglycosides. Do not delay urgent treatment in order to test.
- Monitor renal function and drug concentrations carefully on treatment. Consider regular audiometry for patients on long-term aminoglycoside therapy.
- Report suspected adverse reactions experienced to the Yellow Card scheme AND via the DATIX system

Monitoring Tool

Following the introduction of this guideline an audit will be carried out within one year by Pharmacy/Microbiology to monitor compliance

STANDARDS	%	CLINICAL EXCEPTIONS
All prescriptions for 'EI' gentamicin will be prescribed and monitored according to this guideline	100	See Exclusions

References

1. Joint Formulary Committee. *British National Formulary*. [BNF online]. London: BMJ Group and Pharmaceutical Press. Available from: <http://www.medicinescomplete.com> [Accessed on 18th June 2023].
2. Urban AW, Craig WA. Daily dosage of Aminoglycosides. *Current Clinical Topics in Infectious Diseases Vol 17*, JS Remington & MN Swartz, Eds. Blackwell Science, Malden, MA, 1997
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