ANTIMICROBIAL DOSES FOR ADULTS IN RENAL IMPAIRMENT

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Evidence base	• Renal drug handbook 3rd Edition 2009 • Summary of product characteristics for the individual drugs • Recommended best practice based on clinical experience of guideline developers
Changes from previous Guideline	• Updated dosing advice for a number of antibiotics in line with the updated renal drug handbook 2009 • Removal of the definitions mild, moderate and severe renal failure in line with the BNF • Addition of azithromycin, daptomycin, posaconazole, foscarnet, ganciclovir, valganciclovir, valaciclovir, chloramphenicol and cefalexin
Inclusion criteria	Adult patients with renal impairment
Distribution	- Pharmacists/Medicines Information - Clinical Effectiveness Database - Renal Unit doctors handbook distributed to all SHOs and SpRs - Junior doctors handbook available via the intranet - NUH Antibiotic Guidelines intranet site http://nuhnet/diagnostics_clinical_support/antibiotics
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This guideline has been registered with the Trust.
Clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt contact a senior colleague. Caution is advised when using guidelines after a review date.

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Assessing Renal Function

The Cockcroft-Gault equation (below) should be used to calculate creatinine clearance and gives an estimate of kidney function for the purposes of drug dosing in renal impairment . **Cockcroft-Gault CrCl estimates should be used for drug dosing rather than the automated MDRD eGFR produced by the clinical chemistry laboratory available on NOTIS/HISS. There can be a significant difference between the results of the two calculations.**

$$\text{CrCl (ml/min)} = F \times \frac{(140-\text{age}) \times \text{weight (kg)}}{\text{serum creatinine (micromol/L)}}$$

where F

= 1.23 (male)
= 1.04 (female)

- If patient is anuric, morbidly obese or in acute renal failure (ARF), this equation will NOT give a true reflection of creatinine clearance.
- For those who are morbidly obese, ideal body weight should be calculated
    - IBW for males = 50 + (2.3xheight in inches >60inches);
    - IBW for female = 45 + (2.3xheight in inches>60inches)
- Anuric and oliguric (<500ml/day) patients can be assumed to have a CrCl < 10ml/min (severe renal impairment)

†Many elderly patients have a CrCl below 50ml/min, which, because of reduced muscle mass, may not be indicated by a raised creatinine level. It is therefore especially prudent to calculate the CrCl as outlined above for this patient group**.**

Renal dosing monographs

- The doses recommended are derived from the references stated and represent those commonly used in Nottingham (these may vary from Data Sheet recommendations)
- If 50% quoted, give half the dose but retain the normal frequency
- For dosing advice in haemodialysis (HD) and continuous ambulatory peritoneal dialysis (CAPD) patients at both QMC and NCH: refer to Renal Pharmacist (bleep 80-7078)
- For dosing advice in continuous veno-venous haemofiltration (CVVH): refer to Critical Care Pharmacist (City campus bleep 80-6914 or QMC campus bleep 80-6315)
- Drugs marked * = Contact microbiologist for advice on assays where appropriate.
- The sodium content of some IV antibiotic preparations may be significant (refer to ward pharmacist or Medicines Information)
- **Give post HD (haemodialysis):** If patient is on daily or alternate day therapy this advice refers **only** to administration on dialysis days: ie on non-dialysis days the drug is given at the normal time.

Contact microbiology or pharmacy for advice on dosing in renal impairment for any antimicrobial agents that are not included in the table below

Antimicrobial	Creatinine Clearance (ml/min)			Comments
	50-20	20-10	<10	
***Aciclovir IV**	Normal dose every 12h	Normal dose every 24h	50% of normal dose every 24h	Give post HD
Aciclovir po	Normal	Simplex: 200mg qds Zoster: 800mg tds	Simplex: 200mg bd Zoster: 800mg bd	Give post HD
***Amikacin**	5-6 mg/kg 12h	3-4 mg/kg 24h	2mg/kg 24-48h HD: 5mg/kg post HD and monitor levels	Give post HD Monitor blood levels & adjust dose as req'd
Amoxicillin	Normal	Normal	250mg-1g 8h Endocarditis (refer to microbiology):max 6g per day	Give post HD
Lipid associated Amphotericin IV (Abelcet© and Ambisome©)	Normal- see note below	Normal- see note below	Normal- see note below	For further advice on dosing and administration see antibiotic website, local guidelines and Trust IV guide
	Amphotericin is highly NEPHROTOXIC. Daily monitoring of renal function is essential			
Azithromycin	Normal	Normal	Normal	
Benzylpenicillin	Normal	600mg-2.4g every 6 hours	600mg-1.2g every 6 hours Endocarditis (refer to microbiology): max 4.8g per day	Give post HD
Caspofungin	Normal	Normal	Normal	
Cefalexin	Normal	Normal	250-500mg tds	Give post HD
Cefradine	Normal	Normal	250mg-500mg 6h	Give post HD
Ceftazidime	**CrCl 30-50 ml/min** 1-2g 12h	**CrCl 20-30 ml/min** 1-2g 24h	**CrCl 5-20 ml/min** 500mg-1g 24h **CrCl<5 ml/min** 500mg-1g 48h	Give post HD
Ceftriaxone	Normal	Normal	Normal Max 2g/day	
Cefuroxime IV	Normal	750mg – 1.5g 12h	750mg 12h	Give post HD
Chloramphenicol	Normal	Normal	Normal	
Ciprofloxacin IV+po	Normal	PO 250-500mg bd IV 200mg-400mg bd	PO 250-500mg bd IV 200mg-400mg bd	
Clarithromycin IV + po	Normal	Normal	250-500mg bd	Give post HD
Clindamycin IV +po	Normal	Normal	Normal	
Co-Amoxiclav IV (Augmentin)	CrCl 30-50 Normal	CrCl 10-30 1.2g 12h	1.2g stat then 600-1.2g 12h	Give post HD
Co-Amoxiclav po (Augmentin)	Normal	Normal	Normal	Give post HD
Colistin IV	Normal	50% of normal dose	30% of normal dose	
***Co-trimoxazole IV + po (Treatment doses only)**	**CrCl 30–50 ml/min** Normal	**CrCl 15-30 ml/min** PCP: Normal for 3/7 then 50% Other infections: 50%	**CrCl <15ml/min** All infections: 50%	Give post HD Monitor sulfamethoxazole levels
Daptomycin	**CrCl 30-50ml/min** Normal	**CrCl<30ml/min** 4mg/kg every 48 hours		Not dialysed

Antimicrobial	Creatinine clearance (ml/min)			Comments
	50-20	20-10	<10	
Doxycycline	Normal	Normal	Normal	All other tetracyclines contraindicated in renal impairment
Ertapenem	CrCl 30-50 ml/min Normal	CrCl 10-30 ml/min 50-100% of dose	50% of dose or 1g three times a week	Give post HD
Erythromycin po	Normal	Normal	250-500mg qds	
***Ethambutol**	Normal	7.5-15mg/kg/day	5-7.5mg/kg/day	Give post HD
	Monitor levels if Crcl < 30ml/min (contact Micro)			
Flucloxacillin IV+po	Normal	Normal	Normal Max 4g/day	
Fluconazole	Normal	Normal	50% Oral dose min 50mg	Give post HD No adjustments for single doses required
***Flucytosine**	50mg/kg 12h	50mg/kg 24h	50mg/kg stat then dose according to levels.	Give post HD. Monitor pre-dialysis levels
Foscarnet	Dose reduction required seek further advice from pharmacy/renal drug handbook			
Fusidic acid	Normal	Normal	Normal	
Ganciclovir	Dose reduction required seek further advice from pharmacy/renal drug handbook			
1) Gentamicin **ONCE DAILY**	**CrCl 10–40ml/min** 3mg/kg (max 300mg) Check levels 18-24 hours after first dose. Re-dose only when level < 1mg/L.		**CrCl<10ml/min** 2 mg/kg (max 200mg) re-dose according to levels	BOTH METHODS: Give post HD Monitor blood levels & adjust dose as required. For further advice see monitoring guidance on the antibiotic website http://nuhweb/antibiotics
2) Gentamicin **CONVENTIONAL**	80mg 12h (60mg if <60kg)	80mg 24h (60mg if <60kg)	80mg 48h (60mg if <60kg) HD:1-2 mg/kg post HD redose according to levels	
Isoniazid	Normal	Normal	200mg-300mg 24h	Give post HD
Itraconazole	Normal	Normal	Normal	
Levofloxacin	500mg stat then 250mg bd**	500mg stat then 125mg bd**	500mg stat then 125mg od	** Applies if full dose is 500mg bd. If full dose 500mg **od** give the reduced dose daily
Linezolid	Normal	Normal	Normal	Give post HD
Meropenem Higher doses needed in CNS infection d/w micro	500mg-2g bd	500mg-1g bd	500mg-1g od	Give post HD
Metronidazole	Normal	Normal	Normal	Give post HD
Nitrofurantoin	Use at normal dose with caution	Contraindicated	Contraindicated	Monitor for toxicity e.g blood dyscrasias, neuropathy
Oseltamivir (treatment dose)	**CrCl >30ml/min** 75mg bd	**CrCl 10-30ml/min** 75mg od	30mg stat	HD: 30mg after alternate dialysis sessions
Penicillin V	Normal	Normal	Normal	Give post HD
Piperacillin/ Tazobactam (Tazocin)	Normal	4.5g 8-12h	4.5g 12h	Give post HD
Posaconazole	Normal	Normal	Normal	
Pyrazinamide	Normal	Normal	Normal	
Rifampicin	Normal	Normal	50-100%	

Antimicrobial	Creatinine Clearance (ml/min)			Comments
	50-20	20-10	<10	
Teicoplanin*	Normal	Normal loading dose then 200-400mg every 24-48h	Normal loading dose then 200-400mg every 48-72h	Normal Loading dose 400mg every 12 hours for 3 doses Monitor levels
Tetracycline	Use **Doxycycline** see above			
Tigecycline	Normal	Normal	Normal	
Trimethoprim	Normal	Use alternative agent if possible Normal	Ineffective for UTI, other indications: Normal but use alternative agent if possible	Give post HD Consider short term folic acid supplementation. NB May cause temporary rise in creatinine due to reduced creatinine secretion rather than a fall in CrCl
Valaciclovir	CrCl 30-50ml/min Normal	Dose reduction required for Crcl<30ml/min seek further advice from pharmacy/renal drug handbook		
Valganciclovir	Dose reduction required seek further advice from pharmacy/renal drug handbook			
Vancomycin	1g od Check pre dose level before 3rd dose.	1g 48 h Check pre dose level before 2nd dose	1g stat (or 15mg/kg max 2g). Check level after 4-5 days. ONLY re-dose when level <12mg/L. If deep seated when <15mg/L	Monitor blood levels & adjust dose as required
Voriconazole	Normal	Normal	Normal	Give post HD Caution in the use of IV in renal impairment due to accumulation of vehicle-discuss with pharmacy

Evidence base of guideline

Information derived from standard reference sources:

1. BMA and RPSGB. British National Formulary. Number 57. March 2009
2. Summary of Product Characteristics from electronic Medicines Compendium for individual drugs. Available from http://emc.medicines.org.uk Datapharm Communications Ltd.
3. Ashley C and Currie A. The Renal Drug Handbook. 3rd edition 2009. Radcliffe Publishing Ltd. Oxford.