the children's hospital at Westmead

ANTIMICROBIAL DOSING IN RENAL IMPAIRMENT - CHW

PRACTICE GUIDELINE ©

DOCUMENT SUMMARY/KEY POINTS

- Antimicrobials that are **NOT** renally cleared and/or are **NOT** nephrotoxic should be considered as first line alternatives in patients with renal impairment.
- This is summarised in the quick reference table below. There have been significant updates in antimicrobial dosing for renal impairment and renal replacement therapy for paediatric populations.
- The best equation for estimating glomerular filtration rate (GFR) from serum creatinine in children is the Bedside Schwartz equation for use with creatinine methods with calibration traceable to IDMS.
- Therapeutic drug monitoring is recommended for renally impaired patients on antimicrobial therapy to monitor toxicity and ensure efficacy.
- It should be borne in clinicians' minds that CVVHDF removes drugs more efficiently than CVVHD.

CHANGE SUMMARY

- Significant updates in antimicrobial dosing for renal impairment and renal replacement therapy for paediatric populations: recommended re-reading the entire document.
- Additional antimicrobials have been included in this version.

READ ACKNOWLEDGEMENT

- Clinical staff prescribing and administering antibiotics for patients with renal impairment should read and acknowledge this document.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
Date Effective:	1st January 2016	**Review Period:** 3 years
Team Leader:	Antimicrobial Stewardship Pharmacist	**Area/Dept:** Infectious Diseases

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TABLE OF CONTENTS

1 Antimicrobial Dosing in Renal Impairment – Quick Reference Table

Drug	Route	Dose adjustment for renal impairment (GFR in mL/min)	Peritoneal Dialysis (PD)	Intermittent Haemodialysis (IHD)	Continuous Renal Replacement Therapy (CRRT)
Aciclovir *(Nephrotoxic)* % excreted unchanged in urine: 40-70	PO	**>25 mL/min:** No dose adjustment **25-10 mL/min:** For treatment: 100% 8hrly For prophylaxis: no dose adjustment **<10 mL/min:** For treatment: 100% 12hrly For prophylaxis: 50% 12hrly	**Not Dialysed** For treatment: 100% 12hrly For prophylaxis: 50% 12hrly Give dose after dialysis	**Dialysed** For treatment: 100% 12hrly For prophylaxis: 50% 12hrly Administer after HD on dialysis days	**Dialysed** For treatment: 100% 8hrly For prophylaxis: no dose adjustment
	IV	**>50 mL/min:** No dose adjustment **50-25 mL/min:** 100% 12hrly **25-10 mL/min:** 100% 24hrly **<10 mL/min:** 50% 24hrly	**Not Dialysed** 50% 24hrly No supplement dose needed	**Dialysed** 50% 24hrly Administer after HD on dialysis days	**Dialysed** **CVVH:** 5-10 mg/kg/dose 24hrly **CVVHD/CVVHDF:** 5-10 mg/kg/dose 12-24hrly Note: Higher dose recommended for viral meningoencephalitis and VZV
Amikacin *(Nephrotoxic: Seek specialist advice to consider alternatives)* % excreted unchanged in urine: 95	IV/IM	**>50 mL/min:** No dose adjustment **50-30 mL/min:** 7.5 mg/kg/dose 12hrly **29-10 mL/min:** 7.5 mg/kg/dose 24hrly **<10 mL/min:** 7.5 mg/kg/dose 48-72hrly	**Dialysed** 5 mg/kg/dose Redose as indicated by serum concentrations. Target peak: <30 mg/L Target trough: <2.5 mg/L Redose when peak serum concentration <10 microg/mL	**Dialysed** 5 mg/kg/dose Redose when pre-HD serum concentration <10 mg/L; redose when post-HD serum concentration <6-8 microg/mL Administer after HD on dialysis days	**Dialysed** 7.5 mg/kg/dose 12hrly Monitor serum concentrations Target peak: <30 mg/L Target trough: <2.5 mg/L Redose when peak serum concentration <10 microg/mL

Drug	Route	Dose adjustment for renal impairment (GFR in mL/min)	Peritoneal Dialysis (PD)	Intermittent Haemodialysis (IHD)	Continuous Renal Replacement Therapy (CRRT)
Amphotericin B (liposomal) *(Nephrotoxic: Seek specialist advice to consider alternatives)* % excreted unchanged in urine: 2-5	IV	**Not Dialysed** No dosage adjustment provided in manufacturer's labelling			
Ampicillin % excreted unchanged in urine: 30-80	IV/IM	**50-30 mL/min:** 50 mg/kg/dose 6hrly **29-10 mL/min:** 50 mg/kg/dose 8hrly **<10 mL/min:** 50 mg/kg/dose 12hrly	**Dialysed** 50 mg/kg/dose 12hrly	**Dialysed** 50 mg/kg/dose 12hrly Administer after HD on dialysis days	**Dialysed** CVVH: 50 mg/kg/dose 12hrly CVVHD: 50 mg/kg/dose 8hrly CVVHDF: 50 mg/kg/dose 6-8hrly
Amoxycillin % excreted unchanged in urine: 50-70	PO	**>30 mL/min:** No dose adjustment **29-10 mL/min:** 50% 12hrly **<10 mL/min:** 50% 24hrly	**Dialysed** 50% 24hrly	**Dialysed** 50% 24hrly Administer after HD on dialysis days	**Dialysed** No dose adjustment
Amoxycillin/Clavulanate % excreted unchanged in urine: Amoxycillin 60, clavulanic acid: 40	PO	**>30 mL/min:** No dose adjustment **29-10 mL/min:** 50% 12hrly **<10 mL/min:** 50% 24hrly	**Dialysed** 50% 24hrly	**Dialysed** 50% 24hrly Administer after HD on dialysis days	**Dialysed** 50% 12hrly

Drug	Route	Dose adjustment for renal impairment (GFR in mL/min)	Peritoneal Dialysis (PD)	Intermittent Haemodialysis (IHD)	Continuous Renal Replacement Therapy (CRRT)
Azithromycin % excreted unchanged in urine: 6-12	PO/IV	**No dose adjustment**			
Aztreonam % excreted unchanged in urine: 60-70	IV/IM	**>30 mL/min:** No dose adjustment **29-10 mL/min:** 15-20 mg/kg/dose 8hrly **<10 mL/min:** 7.5-10 mg/kg/dose 12hrly	**Dialysed** 7.5-10 mg/kg/dose 12hrly	**Dialysed** 7.5-10 mg/kg/dose 12hrly Administer after HD on dialysis days	**Dialysed** No dose adjustment
Benzylpenicillin % excreted unchanged in urine: 60-90	IV/IM	**Uraemic and >10 mL/min:** Load 1 dose at 100% then 50% 4hrly **<10 mL/min:** Load 1 dose at 100% then 50% 8hrly	**Dialysed** Give 1 dose at 100% then 50% 8hrly	**Dialysed** 50% q4-6hrly Administer after HD on dialysis days	**Dialysed** **CVVH**: Load 60 mg/kg/dose, then 30 mg/kg/dose 4-6hrly **CVVHD**: Load 60 mg/kg/dose, then 30-45 mg/kg/dose 4-6hrly **CVVHDF:** Load 60 mg/kg/dose, then 30-60 mg/kg/dose 4-6hrly
Caspofungin % excreted unchanged in urine: 1.4	IV	**No dose adjustment**			

Drug	Route	Dose adjustment for renal impairment (GFR in mL/min)	Peritoneal Dialysis (PD)	Intermittent Haemodialysis (IHD)	Continuous Renal Replacement Therapy (CRRT)
Cefazolin % excreted unchanged in urine: 80- 100	IV/IM	**>70 mL/min:** No dose adjustment **70-40 mL/min:** 60% 12hrly **40-20 mL/min:** 25% 12hrly **20-5 mL/min:** 10% 24hrly	**Dialysed** 25 mg/kg/dose 24hrly	**Dialysed** 25 mg/kg/dose 24hrly Administer after HD on dialysis days	**Dialysed** 25 mg/kg/dose 8hrly
Cefepime % excreted unchanged in urine: 85	IV/IM	**>50 mL/min:** No dose adjustment **50-10 mL/min:** 50 mg/kg/dose 24hrly **<10 mL/min:** 50 mg/kg/dose 48hrly	**Dialysed** 50 mg/kg/dose 24hrly	**Dialysed** 50 mg/kg/dose 24hrly	**Dialysed** 50 mg/kg/dose 12hrly
Cefotaxime % excreted unchanged in urine: 40-60	IV/IM	**50-30 mL/min:** 35 mg/kg/dose 8-12hrly **29-10 mL/min:** 35 mg/kg/dose 12hrly **<10 mL/min:** 35 mg/kg/dose 24hrly	**Dialysed** 35 mg/kg/dose 24hrly	**Dialysed** 35 mg/kg/dose 24hrly Administer after HD on dialysis days	**Dialysed** **CVVH**: 25-50 mg/kg/dose 8-12hrly **CVVHD**: 25-50 mg/kg/dose 8hrly **CVVHDF**: 25-50 mg/kg/dose 6-8hrly

Drug	Route	Dose adjustment for renal impairment (GFR in mL/min)	Peritoneal Dialysis (PD)	Intermittent Haemodialysis (IHD)	Continuous Renal Replacement Therapy (CRRT)
Ceftazidime % excreted unchanged in urine: 60-80	IV/IM	**>50 mL/min:** No dose adjustment **50-30 mL/min:** 50 mg/kg/dose 12hrly **29-10 mL/min:** 50 mg/kg/dose 24hrly **<10 mL/min:** 50 mg/kg/dose 48hrly	**Dialysed** 50 mg/kg/dose 48hrly	**Dialysed** 50 mg/kg/dose 48hrly Administer after HD on dialysis days	**Dialysed** 50 mg/kg/dose 12hrly CVVHDF and GNR MIC>4: Load 50 mg/kg/dose, then give 75 mg/kg/day as a 24 hour continuous infusion
Ceftriaxone % excreted unchanged in urine: 40-60	IV/IM	**No dose adjustment**	**Poorly dialyzed; no supplemental dose or dosage adjustment necessary, including patients on IHD, PD, or CRRT**		
Cefuroxime % excreted unchanged in urine: 90	PO	**>30 mL/min:** No dose adjustment **10-29 mL/min:** 100% 12hrly **<10 mL/min:** 100% 24hrly	**Dialysed** 100% 24hrly	**Dialysed** 100% 24hrly Administer after HD on dialysis days	**No dose adjustment**
Cefalexin % excreted unchanged in urine: 80-90	PO	**40-10 mL/min:** 100% 8hrly **<10 mL/min:** 100% 12- 24hrly	**Dialysed** 100% 12hrly	**Dialysed** 100% 12hrly Administer after HD on dialysis days	**Dialysed** 100% 12hrly

Drug	Route	Dose adjustment for renal impairment (GFR in mL/min)	Peritoneal Dialysis (PD)	Intermittent Haemodialysis (IHD)	Continuous Renal Replacement Therapy (CRRT)
Cidofovir *(Nephrotoxic: Seek specialist advice to consider alternatives)* % excreted unchanged in urine: 80-100	IV	**If SrCr >132 µmol/L, CrCl <90 mL/min and >2+ proteinurea:** Induction: 1mg/kg/dose 3 times weekly on alternate days for 2 consecutive weeks Maintenance: 1 mg/kg/dose every 2 weeks	**Not Dialysed** Give 0.5 mg/kg/dose	**Dialysed** Give 0.5 mg/kg/dose Give 2 hours before dialysis session	**Unknown dialysability** Give 0.5 mg/kg/dose
Ciprofloxacin % excreted unchanged in urine: 40-70	IV/PO	**>30 mL/min:** No dose adjustment **29-10 mL/min:** 10-15 mg/kg/dose q18hrly **<10 mL/min:** 10-15 mg/kg/dose 24hrly	**Not Dialysed** 10-15 mg/kg/dose 24hrly	Not **Dialysed** 10-15 mg/kg/dose 24hrly Administer after HD on dialysis days	**Dialysed** 10-15 mg/kg/dose 12hrly
Clarithromycin % excreted unchanged in urine: 15-40	PO	**>30 mL/min:** No dose adjustment **29-10 mL/min:** 4 mg/kg/dose 12hrly **<10 mL/min:** 4 mg/kg/dose 24hrly	**Unknown dialysability** 4 mg/kg/dose 24hrly	**Dialysed** 4 mg/kg/dose 24hrly Administer after HD session is completed	**Unknown dialysability** 4 mg/kg/dose 12hrly
Clindamycin % excreted unchanged in urine: 10	IV/IM	**No adjustment required**	**Not dialyzable (0% to 5%)** **No adjustment required**		

Drug	Route	Dose adjustment for renal impairment (GFR in mL/min)	Peritoneal Dialysis (PD)	Intermittent Haemodialysis (IHD)	Continuous Renal Replacement Therapy (CRRT)
Colistin *(Nephrotoxic: Seek specialist advice to consider alternatives)* % excreted unchanged in urine:80	IV	**>80 mL/min:** No dosage adjustment necessary **50-79 mL/min:** 1.25-1.9 mg/kg/dose 12hrly **30-49 mL/min:** 1.25 mg/kg/dose 12hrly **10-29 mL/min:** 1.5 mg/kg/dose 36 hrly **<10 mL/min:** 1.5 mg/kg 48 hrly	**Dialysed** 1.5 mg/kg 48 hrly	**Not Dialysed** 1.5 mg/kg 48 hrly Administer after hemodialysis on dialysis days	**Dialysed** 2.5 mg/kg 24-48hrly
Dapsone % excreted unchanged in urine: 20		**>10 mL/min:** No adjustment required **<10 mL/min:** 1-2 mg/kg/dose daily	**Likely to be Dialysed** 1-2 mg/kg/dose daily	**Dialysed** 1-2 mg/kg/dose daily	**Likely to be Dialysed** No dose adjustment
Daptomycin % excreted unchanged in urine: 50	IV	**>30 mL/min:** No dose adjustment **29-10 mL/min:** 67% 24hrly **<10 mL/min:** 67% 48hrly	**Not Dialysed** 67% 48hrly	**Not Dialysed** 67% 48hrly	**Slightly Dialysed** 8 mg/kg/dose 48 hrly
Doxycycline % excreted unchanged in urine: 33-4	PO	**No dose adjustment**			

Drug	Route	Dose adjustment for renal impairment (GFR in mL/min)	Peritoneal Dialysis (PD)	Intermittent Haemodialysis (IHD)	Continuous Renal Replacement Therapy (CRRT)
Ertapenem % excreted unchanged in urine: 38	IV/IM	**>30 mL/min:** No dose adjustment **<30 mL/min:** 15mg/kg/dose 24hrly	**Dialysed** 15 mg/kg/dose 24 hrly	**Dialysed** 15mg/kg/dose 24hrly	**Dialysed** No dose adjustment
Erythromycin % excreted unchanged in urine: 2-15	PO/IV	**>10 mL/min:** No dose adjustment **<10 mL/min:** 10-17 mg/kg/dose 8hrly	**Not Dialysed** 10-17 mg/kg/dose 8hrly	**Not Dialysed** 10-17 mg/kg/dose 8hrly	**Slightly dialyzable (5% to 20%);** No dose adjustment
Flucloxacillin % excreted unchanged in urine: 66-76	IV/IM/ PO	**>10 mL/min:** No adjustment required <10 mL/min and IV: 50% 4-6hrly	**Not Dialysed** 50% 4-6hrly	**Not Dialysed** 50% 4-6hrly	**Not Dialysed** No adjustment required
Fluconazole % excreted unchanged in urine: 80	PO/IV	**>50 mL/min:** No adjustment required **50-10 mL/min:** Load 100%, then 50% 24hrly **<10 mL/min:** Load 100%, then 50% 48hrly	**Dialysed** Load 100%, 50% 48hrly	**Dialysed** No dose adjustment After each dialysis session	**Dialysed** Load 100%, 6 mg/kg/dose 24hrly
Flucytosine % excreted unchanged in urine: 90	IV	**Dose according to levels Target trough of 25-50 µg/mL** **50-30 mL/min:** 25-37.5 mg/kg/dose 8hrly **29-10 mL/min:** 25-37.5 mg/kg/dose 12hrly **<10 mL/min:** 25-37.5 mg/kg/dose 24 hrly	**Dialysed** Dose according to levels Target trough of 25-50 µg/mL 25-37.5mg/kg/dose 24hrly	**Dialysed** Dose according to levels Target trough of 25-50 µg/mL 25-37.5mg/kg/dose 24hrly	**Dialysed** Dose according to levels Target trough of 25-50 µg/mL 25-37.5mg/kg/dose 8hrly

Drug	Route	Dose adjustment for renal impairment (GFR in mL/min)	Peritoneal Dialysis (PD)	Intermittent Haemodialysis (IHD)	Continuous Renal Replacement Therapy (CRRT)
Foscarnet *(Nephrotoxic: Seek specialist advice to consider alternatives)* % excreted unchanged in urine: 85	IV	**>50 mL/min:** No adjustment required **50-20 mL/min:** 28 mg/kg/dose 8hrly **20-10 mL/min:** 15 mg/kg/dose 8hrly **<10 mL/min:** 6 mg/kg/dose 8hrly	**Dialysed** 6 mg/kg/dose 8hrly	**Dialysed** 6 mg/kg/dose 8hrly	**Dialysed** 15 mg/kg/dose 8hrly
Ganciclovir (Nephrotoxic) % excreted unchanged in urine: 85-95	PO/IV	**69-50 mL/min:** Induction: 2.5 mg/kg/dose 12hrly Maintenance: 2.5 mg/kg/dose 24hrly **49-25 mL/min:** Induction: 2.5 mg/kg/dose 24hrly Maintenance: 1.25 mg/kg/dose 24hrly **24-10 mL/min:** Induction: 1.25 mg/kg/dose 24hrly Maintenance: 0.625 mg/kg/dose 24hrly **<10 mL/min:** Induction: 1.25 mg/kg/dose 3 times/week Maintenance: 0.625 mg/kg/dose 3 times/week	**Dialysed** Induction: 1.25 mg/kg/dose 3 times/week Maintenance: 0.625 mg/kg/dose 3 times/week	**Dialyzable (50%)** Administer after hemodialysis on dialysis days) CMV Infection: I.V.: Induction: 1.25 mg/kg every 48-72 hours; Maintenance: 0.625 mg/kg every 48-72 hours.	**Dialysed** **CVVH**: Induction: 2.5 mg/kg/dose 24hrly; Maintenance: 1.25 mg/kg/dose 24hrly **CVVHD/CVVHDF**: Induction: 2.5 mg/kg/dose 12 hrly; Maintenance: 2.5 mg/kg/dose 24hrly

Drug	Route	Dose adjustment for renal impairment (GFR in mL/min)	Peritoneal Dialysis (PD)	Intermittent Haemodialysis (IHD)	Continuous Renal Replacement Therapy (CRRT)
Gentamicin *(Nephrotoxic: Seek Infectious Disease specialist advice to consider alternatives)* % excreted unchanged in urine: 95	IV/IM	**Suggest measuring Area Under the Curve (AUC) for once daily dosing.** **Contact the AMS Pharmacist** **≥50 mL/min:** No adjustment required **50-30 mL/min:** 2.5 mg/kg/dose 12hrly **29-10 mL/min:** 2.5 mg/kg/dose 24hrly **<10 mL/min:** 2.5 mg/kg/dose 48-72hrly	**Dialysed** 2 mg/kg/dose 48-72hrly; **Redose as indicated by serum concentration** **Target trough <1 mg/L** **Target peak 6-10 mg/L** **Suggest Measuring Area Under the Curve (AUC).** **Contact the AMS pharmacist**	**Dialysed** 2 mg/kg/dose 48-72hrly; 30 minutes before HD; **Redose as indicated by serum concentration (usually 48hrly)** **Target trough <1 mg/L** **Target peak 6-10 mg/L** **Suggest Measuring Area Under the Curve (AUC).** **Contact the AMS pharmacist**	**Dialysed** 2-2.5 mg/kg/dose 24hrly, **Monitor serum concentrations** **Target trough <1 mg/L** **Target peak 6-10 mg/L** **Suggest Measuring Area Under the Curve (AUC).** **Contact the AMS pharmacist**
Imipenem/Cilastin % excreted unchanged in urine:20-75	IV/IM	**Do not use if <30kg and <50 mL/min** **50-30 mL/min:** 7-13 mg/kg/dose 8hrly **29-10 mL/min:** 7.5-12.5 mg/kg/dose 12hrly **<10 mL/min:** 7.5-12.5 mg/kg/dose 24hrly	**Dialysed** 7.5-12.5 mg/kg/dose 24hrly	**Dialysed** 7.5-12.5 mg/kg/dose 24hrly Administer after HD on dialysis days	**Dialysed** 7-13 mg/kg/dose 8hrly Resistant organisms MIC>4: 12.5 mg/kg/dose 6hrly
Itraconazole % excreted unchanged in urine: 0.03	PO	**No dosage adjustments are required in renal impairment. Dose according to trough levels**			

Drug	Route	Dose adjustment for renal impairment (GFR in mL/min)	Peritoneal Dialysis (PD)	Intermittent Haemodialysis (IHD)	Continuous Renal Replacement Therapy (CRRT)
Lincomycin % excreted unchanged in urine: 2-30	IV/IM	**>50 mL/min:** No dose adjustment **50-10 mL/min:** 100% 12hrly **<10 mL/min:** 100% 24hrly	**Not Dialysed** 100% 24hrly	**Not Dialysed** 100% 24hrly Administer after HD on dialysis days	**Unknown dialysability** 100% 12hrly
Linezolid % excreted unchanged in urine:30	PO/IV	**>10 mL/min:** No dose adjustment **<10 mL/min** Reduce dose to 10 mg/kg/dose 24hrly if platelet count drops	**Dialysed** 10 mg/kg/dose 12hrly Reduce dose to 10 mg/kg/dose 24hrly if platelet count drops	**Dialysed** 10 mg/kg/dose 12hrly Administer after HD on dialysis days Reduce dose to 10 mg/kg/dose 24hrly if platelet count drops	**Dialysed** No adjustment required
Meropenem % excreted unchanged in urine:70	IV	**>50 mL/min:** No adjustment required **50-30 mL/min:** 20-40 mg/kg/dose 12hrly **29-10 mL/min:** 10-20 mg/kg/dose 12hrly **<10 mL/min:** 10-20 mg/kg/dose 24hrly	**Dialysed** 10-20 mg/kg/dose 24hrly	**Dialysed** 10-20 mg/kg/dose 24hrly Administer after HD on dialysis days	**Dialysed** 20-40 mg/kg/dose 12hrly
Metronidazole % excreted unchanged in urine:20	IV/PO	**>10 mL/min:** No adjustment required **<10 mL/min:** 4 mg/kg/dose 6hrly	**Extensively removed by peritoneal dialysis:** 4 mg/kg/dose 6hrly	**Extensively removed by hemodialysis:** 4 mg/kg/dose 6hrly	**No adjustment required**

Drug	Route	Dose adjustment for renal impairment (GFR in mL/min)	Peritoneal Dialysis (PD)	Intermittent Haemodialysis (IHD)	Continuous Renal Replacement Therapy (CRRT)
Moxifloxacin % excreted unchanged in urine:19	IV/PO	**No dosage adjustment required in renal impairment**	**No supplemental dose or dosage adjustment necessary, including patients on IHD, PD, or CRRT**		
Nitrofurantoin *(Nephrotoxic: Seek specialist advice to consider alternatives)* % excreted unchanged in urine:30-40	PO	**>60 mL/min:** No adjustment required **<60 mL/min:** Contra-indicated	**Dialysed** Avoid contra-indicated May cause neuropathy and blood dyscrasias		
Oseltamivir % excreted unchanged in urine: negligible (active metabolites >99)	PO	**>30 mL/min** No adjustment required **10-30 mL/min:** Treatment: 3 mg/kg/dose 24hrly Prophylaxis: 3mg/kg/dose 48hrly **<10 mL/min:** Treatment: 3 mg/kg/dose ONCE ONLY Prophylaxis: 3mg/kg/dose every 10 days.	**Dialysed** Treatment: 3 mg/kg/dose ONCE ONLY Prophylaxis: 3mg/kg/dose every 10 days.	**Dialysed** <15 kg: 7.5mg/dose 15-23 kg: 10 mg/dose 23-40 kg: 15 mg/dose >40 kg: 30 mg/dose Administer only on HD days after HD	**Dialysed** Treatment: 3 mg/kg/dose 24hrly Prophylaxis: 3mg/kg/dose 48hrly
Phenoxymethylpenicillin (Penicillin V) % excreted unchanged in urine: 80-90	PO	**No dosage adjustment required in renal impairment**	**No supplemental dose or dosage adjustment necessary, including patients on IHD, PD, or CRRT**		

Drug	Route	Dose adjustment for renal impairment (GFR in mL/min)	Peritoneal Dialysis (PD)	Intermittent Haemodialysis (IHD)	Continuous Renal Replacement Therapy (CRRT)
Piperacillin/Tazobactam % excreted unchanged in urine: 60-80	IV	**>50 mL/min:** No adjustment required **50-30 mL/min:** 35-50 mg/kg/dose (piperacillin) 6hrly **<30 mL/min:** 35-50 mg/kg/dose (piperacillin) 8hrly	**Peritoneal dialysis removes 21% of tazobactam and 6% of piperacillin:** 50-75 mg/kg/dose (piperacillin) 12hrly	**Hemodialysis removes 30% to 40%:** 50-75 mg/kg/dose (piperacillin) 12hrly Administer after HD on dialysis days	**Dialysed** 35-50 mg/kg (piperacillin) 8hrly
Posaconazole % excreted unchanged in urine: 0.2	PO	**No adjustment required** Patients with CrCl <20 mL/min/1.73 m^2 should be monitored for breakthrough fungal infections Dose according to levels. Target trough for prophylaxis: >700ng/mL Target trough for treatment: >1250ng/mL	**Not Dialysed** Dose according to levels. Target trough for prophylaxis: >700 ng/mL Target trough for treatment: >1250 ng/mL		
Moxifloxacin % excreted unchanged in urine: 19	IV/PO	**No adjustment required**	**Poorly dialyzed; no supplemental dose or dosage adjustment necessary, including patients on IHD, PD, or CRRT**		
Rifampicin % excreted unchanged in urine: 15-30	IV/PO	**No adjustment required**	**Poorly dialyzed; no supplemental dose or dosage adjustment necessary, including patients on IHD, PD, or CRRT**		
Roxithromycin % excreted unchanged in urine: 7	PO	**No adjustment required**	**Not Dialysed** No adjustment required	**Not Dialysed** No adjustment required Administer after HD on dialysis days	**Not Dialysed** No adjustment required

Drug	Route	Dose adjustment for renal impairment (GFR in mL/min)	Peritoneal Dialysis (PD)	Intermittent Haemodialysis (IHD)	Continuous Renal Replacement Therapy (CRRT)
Teicoplanin (Nephrotoxic) % excreted unchanged in urine: >97	IM/IV	Dose according to levels. Target trough 10-20 mg/L Target peak (1hr): 20-50 mg/L **10-20 mL/min:** Load 10 mg/kg/dose 12 hrly for 3 doses then 3-6 mg/kg/dose 48 hrly **<10 mL/min:** Load 10 mg/kg/dose 12 hrly for 3 doses then 3-6 mg/kg/dose 72 hrly	**Not Dialysed** Load 10 mg/kg/dose 12 hrly for 3 doses then 3-6 mg/kg/dose 72 hrly Dose according to levels. Target trough 10-20 mg/L Target peak (1hr): 20-50 mg/L		**Unknown dialysability** Load 10 mg/kg/dose 12 hrly for 3 doses then 3-6 mg/kg/dose 48 hrly Dose according to levels. Target trough 10-20 mg/L Target peak (1hr): 20-50 mg/L
Terbinafine % excreted unchanged in urine: 0	PO	**>50 mL/min:** No adjustment required <50 mL/min: 50% of normal dose	**Unknown dialysability** 50% of normal dose		
Ticarcillin/clavulanate % excreted unchanged in urine: 40-90	IV	**>30 mL/min:** No adjustment required **29-10 mL/min:** 50-75 mg/kg 8hrly (ticarcillin) **<10 mL/min:** 50-75 mg/kg 12hrly (ticarcillin) **<10 mL/min with hepatic failure:** 50-75 mg/kg 24hrly (ticarcillin)	**Not Dialysed** 50-75 mg/kg 12hrly (ticarcillin) PD with hepatic failure: 50-75 mg/kg 24hrly (ticarcillin)	**Dialysed** 50-75 mg/kg 12hrly (ticarcillin) IHD with hepatic failure: 50-75 mg/kg 24hrly (ticarcillin)	**Dialysed** 50-75 mg/kg 8hrly (ticarcillin) Note: Do not administer in intervals exceeding every 8 hours. Clavulanate component is hepatically eliminated; extending the dosing interval beyond 8 hours may result in loss of beta-lactamase inhibition.

Drug	Route	Dose adjustment for renal impairment (GFR in mL/min)	Peritoneal Dialysis (PD)	Intermittent Haemodialysis (IHD)	Continuous Renal Replacement Therapy (CRRT)
Tobramycin (Nephrotoxic: Seek specialist advice to consider alternatives) % excreted unchanged in urine:90	IV/IM	**Suggest measuring Area Under the Curve (AUC) for once daily dosing.** **Contact the AMS Pharmacist** **≥50 mL/min:** No adjustment required **50-30 mL/min:** 2.5 mg/kg/dose 12hrly **29-10 mL/min:** 2.5 mg/kg/dose 24hrly **<10 mL/min:** 2.5 mg/kg/dose 48-72hrly	**Dialysed** 2 mg/kg/dose 48-72hrly; **Redose as indicated by serum concentration** **Target trough <1 mg/L** **Target peak 6-10 mg/L** **Suggest Measuring Area Under the Curve (AUC).** **Contact the AMS pharmacist**	**Dialysed** 2 mg/kg/dose 48-72hrly; 30 minutes before HD; **Redose as indicated by serum concentration (usually 48hrly)** **Target trough <1 mg/L** **Target peak 6-10 mg/L** **Suggest Measuring Area Under the Curve (AUC).** **Contact the AMS pharmacist**	**Dialysed** 2-2.5 mg/kg/dose 24hrly, **Monitor serum concentrations** **Target trough <1 mg/L** **Target peak 6-10 mg/L** **Suggest Measuring Area Under the Curve (AUC).** **Contact the AMS pharmacist**
Trimethoprim/ Sulfamethoxazole % excreted unchanged in urine:15-60	IV/PO	**>30 mL/min:** No change **15-30 mL/min:** 50% of the dose **<15 mL/min:** 50% 48hrly	**Not significantly Dialysed** Prophylaxis: 2.5 mg/kg/dose (TMP) after each dialysis session Treatment: 5-10 mg/kg (TMP) 24hrly after each dialysis session	**Dialysed** Prophylaxis: 2.5 mg/kg/dose (TMP) after each dialysis session Treatment: 5-10 mg/kg (TMP) 24hrly after each dialysis session	**Dialysed** Prophylaxis: 50% of the dose Treatment: 5 mg/kg/dose (TMP) 8hrly
Valaciclovir (Nephrotoxic) % excreted unchanged in urine: <1 Converted to acyclovir as 88% in urine	PO	**50-30 mL/min:** No change **15-29 mL/min:** 100% 12hrly **<15 mL/min:** 50% 24hrly	**Probably Dialysed** 50% 24hrly	**Dialysed** 50% 24hrly	**Probably Dialysed** 100% 12hrly

Drug	Route	Dose adjustment for renal impairment (GFR in mL/min)	Peritoneal Dialysis (PD)	Intermittent Haemodialysis (IHD)	Continuous Renal Replacement Therapy (CRRT)
Vancomycin (Nephrotoxic) % excreted unchanged in urine: 80-90	IV	**Base on trough levels. Target trough 10-20 mg/L** **50-30 mL/min:** 10-15 mg/kg/dose 12hrly **29-10 mL/min:** 10-15 mg/kg/dose 24hrly **<10 mL/min:** 10-15 mg/kg/dose **Re-dose based on serum concentrations**	**Not Dialysed** 10-15 mg/kg/dose **Re-dose based on serum concentrations**	**Not Dialysed** **Re-dosing based on pre-HD serum concentrations:** **<10 mg/L:** 15 mg/kg/dose after HD **10-20 mg/L:** 7.5 mg/kg/dose after HD **>20 mg/L:** Hold vancomycin **Re-dosing based on post-HD serum concentrations:** **<10-15 mg/L:** 7.5-15 mg/kg/dose	**Dialysability unknown** **Re-dose based on serum concentrations** **CVVH:** Loading dose of 25 mg/kg, then by 10-15 mg/kg/dose every 24-48hrly **CVVHD:** Loading dose of 25 mg/kg, then by 10-15 mg/kg 24hrly **CVVHDF:** Loading dose of 25 mg/kg, then by 7.5-10 mg/kg 12hrly
Valganciclovir (Nephrotoxic) % excreted unchanged in urine: 85-95 as ganciclovir **REFER TO Section 2.4**	PO	**>10 mL/min:** Use BSA formula Prevention: 7x BSA x CrCl = 24hrly dose in mg (Max. 900 mg/day) Treatment: 7x BSA x CrCl = 12hrly dose in mg (Max. 1800 mg/day) **<10 mL/min:** Use ganciclovir	**Dialysed** Valganciclovir is not recommended. Use ganciclovir	**Dialysed** Valganciclovir is not recommended. Use ganciclovir	**Probably Dialysed** Prevention: 9 mg/kg/dose twice a week (Max. 450 mg/dose) Treatment: 9 mg/kg/dose 48hrly (Max. 450 mg/dose)

Drug	Route	Dose adjustment for renal impairment (GFR in mL/min)	Peritoneal Dialysis (PD)	Intermittent Haemodialysis (IHD)	Continuous Renal Replacement Therapy (CRRT)
Voriconazole % excreted unchanged in urine: <2 (IV formulation contains nephrotoxic vehicle)	IV	**>50 mL/min:** No adjustment required **<50 mL/min:** Accumulation of the intravenous vehicle occurs. After initial I.V. loading dose, oral voriconazole should be administered, unless an assessment of the risk: benefit justifies the use of I.V. voriconazole. Monitor serum creatinine and change to oral voriconazole therapy when possible.	**Poorly dialyzed; no supplemental dose or dosage adjustment necessary, including patients on IHD, PD, or CRRT** Monitor serum creatinine and change to oral voriconazole therapy when possible.		
	PO	**No adjustment required**			

2 Aminoglycoside & Vancomycin Dosing in Dialysis

2.1 Aminoglycosides (Gentamicin, Tobramycin and Amikacin)

Aminoglycosides are small hydrophilic molecules with low protein binding and low volume of distribution in patients with normal renal function. They are entirely renally cleared and thus the half-life increases from 2 – 3 hours in normal renal function to 50 – 70 hours in renal failure patients. Intermittent haemodialysis in acute renal injury is effective in the removal of this class of antibiotics.

Aminoglycosides display concentration-dependent killing and minimum target peak levels are recommended depending on the agent being used. Therapeutic drug monitoring must be done for patients on aminoglycosides with impaired renal function. Adequate peak concentrations (6-10 mg/L) must be attained in order to achieve good clinical outcomes. The area under the curve (AUC)/minimum inhibitory concentration (MIC) or peak/MIC ratio are the most important predictors of efficacy. Target AUC is 70-120mg.h/L. Target trough level is <1 mg/L (single daily dosing) or <2mg/L (multiple day dosing) and should be monitored prior to re-dosing. For AUC monitoring please contact the Antimicrobial Stewardship pharmacist on pager 6658.

In critically ill patients, volume of distribution is increased - this may result in the need for higher than usual recommended doses. One adult population pharmacokinetic study suggests that using a dose of 6 mg/kg and extending the dosing interval to 48 hourly provides the best solution to achieving optimal peak and safe trough levels, in their cohort of critically ill patients.[6] Similar paediatric studies are not available, however as the usual recommended adult dose is 5 mg/kg (30 – 60 years), to ensure adequate peak serum aminoglycoside levels in critically ill paediatric patients receiving dialysis, dosing should not be reduced beyond that currently recommended for age and weight (6 – 7.5 mg/kg age dependent) while extending the dosing interval. Aminoglycoside serum level should be monitored prior to administration of further doses in patients with severe renal impairment or receiving dialysis.

Aminoglycosides **ARE NOT** agents of first choice in patients with renal impairment, however in the emergency setting where the organism is unknown or where no other alternative is available due to resistant organism in patients receiving haemodialysis, **aminoglycoside dose should be administered 30 mins prior to the commencement of IHD**. This allows attainment of a high peak level and then utilises rapid drug clearance to minimise the trough level and optimise the area under the curve (AUC). Extending the dosing interval rather than reducing the dose is recommended to ensure that the appropriate serum levels to ensure safety and minimise toxicity.

Please refer to the reference table for dosing guidelines

2.2 Vancomycin

Vancomycin is a large molecule and is well distributed in body tissues. Protein binding in severe renal dysfunction is reduced from 55% to approximately 20%, with half-life increasing from 6 hours in normal renal function to > 168 hours in anephric patients. Vancomycin is poorly removed by low-flux membranes, whereas high flux membranes significantly remove the drug by 30-46%.

To ensure treatment efficacy and reduce the development of resistance, the current recommendation for therapeutic trough serum levels is 10 – 20 mg/L (15 – 20 mg/L in severe or deep tissue infection). There seems to be a causal link between prolonged low serum vancomycin levels and the emergence of VISA (Vancomycin intermediate Staph Aureus) and hVISA (heterogenous VISA).

Please note: *as the following suggested dosing regimen are an extrapolation of adult data (similar paediatric data unavailable) – they are given as a guide only as they have not been validated in the paediatric setting. Actual dose and dosing intervals should be based on close monitoring of serum vancomycin levels.*

2.3 Dosing guidelines

Haemodialysis

1. **Dosing** is based on pre-dialysis vancomycin serum level as follows:

Level	Recommended Dose
>20 mg/L	no dose to be administered
10-20 mg/L	7.5 mg/kg/dose after HD
<10 mg/L	15 mg/kg/dose after HD

Continuous renal replacement therapy (CRRT)

CRRT effectively removes vancomycin. Specifically CVVHDF (continuous venovenous haemodiafiltration) removes vancomycin to a greater degree than CVVH (continuous venovenous hemofiltration) and CVVHD (continuous venovenous haemodialysis).

1. **Loading dose** – 25 mg/kg/dose
2. **Subsequent dose** interval should be decided based on serum level.

   Re-dose at serum levels < 15mg/L

   Suggested dosing regimen:

   CVVH: 10 – 15 mg/kg/dose 24 – 48 hourly

   CVVHD: 10 – 15 mg/kg/dose 24 hourly

   CVVHDF: 7.5 – 10 mg/kg/dose 12 hourly

2.4 Valganciclovir Dosing Calculation

Valganciclovir is a pro-drug of ganciclovir, which inhibits replication of herpes viruses, including cytomegalovirus (CMV), herpes simplex virus types 1 and 2. It is indicated for the treatment and prophylaxis of CMV infection following solid organ transplantation in patients at risk of CMV disease and in the treatment of CMV retinitis in AIDS.

For patients aged **4 month to 16 years**:

Paediatric dose (mg) = 7 x BSA x Creatinine Clearance mL/min/1.73m^2 *

**(calculated using the Bedside Schwartz formula)*

When calculating the paediatric dose, a maximum creatinine clearance value of 75 mL/min/1.73m^2 should be used, even if the calculated Bedside Schwartz creatinine clearance exceeds this value. This will ensure appropriate dosing in the paediatric population and will help avoid the potential for ganciclovir overexposure due to low body weight, low body surface area and very low serum creatinine.

Body Surface Area (m^2) = [(Height (m) x Weight (kg)) / 3600]^{½}

The Bedside IDMS-traceable Schwartz formula for determining creatinine clearance is:

GFR (mL/min/1.73 m^2) = (36.5 × Height in cm) / Creatinine in micromol/L

Maximum single dose should not exceed 900 mg regardless of calculated dose. All calculated doses should be rounded to the nearest 25 mg for a convenient deliverable dose. If the calculated dose is within 10% of the available tablet strength, one 450 mg tablet may be taken (e.g. between 405 and 495 mg)

For further advice on dosing and monitoring, contact ward pharmacist or Antimicrobial Stewardship pharmacist on page no. 6658.

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