

RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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Antibiotics in renal impairment

Confusion surrounds the prescribing of antimicrobials in renal impairment; whether to reduce the dose or extend the dosing interval. Suggested dose adjustments in renal impairment for many commonly used antibiotics are provided here, based on tables which can be found in the Therapeutic Guidelines (TG) Antibiotic, 14th edition. No dose adjustment is required for some agents – these include azithromycin, roxithromycin, ceftriaxone, cefaclor, clindamycin, doxycycline, linezolid, moxifloxacin, phenoxymethylpenicillin, metronidazole among others. The dosing of antibiotics such as penicillins (beta-lactams) and vancomycin is time-dependent, meaning that these exert optimal bactericidal effect when drug concentrations are maintained above the minimum inhibitory concentration (MIC). Therefore reducing the frequency of administration by extending the dosing interval (rather than changing the magnitude of individual doses) is the strategy for dosing these antibiotics in renal impairment. Concentration-dependent antibiotics achieve increasing bactericidal action with increasing levels of drug. In addition, these agents have an associated concentration-dependent post-antibiotic effect in which bactericidal action continues for a period of time after the antibiotic level falls below the MIC. Therefore the magnitude of the individual dose given is important. Area under the curve (AUC) methods are commonly used to calculate total exposure to aminoglycosides, while for other concentration-dependent antibiotics (fluoroquinolones, azithromycin and metronidazole) AUC calculations are not performed.

Penicillins - Penicillins have quite a large therapeutic window; doses generally only need to be significantly adjusted for GFR < 10ml/min.

	GFR 10-50mL/min	GFR <10mL/min
Amoxycillin	100% 8-12 hourly	100% 24-hourly
Ampicillin	100% 8-12 hourly for GFR<30	100% 12-24 hourly
benzylpenicillin (penicillin G)	75% dose at normal interval	20-50% dose at normal interval
Flucloxacillin or dicloxacillin	Normal	0.25-1g 6-8 hourly

Beta-lactamase inhibitors are also renally cleared. The Therapeutic Guidelines advocate extended dosing interval for combination products as follows: amoxycillin/clavulanate: 500/125mg 12-hrly for GFR <30ml/min (and once per 24 hours if the GFR <10ml/min as per the product information); piperacillin/tazobactam: 100% dose 12-hourly for GFR < 20ml/min; ticarcillin/clavulanate: 100% dose 8-12 hourly for GFR 10-30mL/min, 12-hourly for GFR <10mL/min (while the product information recommends reducing dose to 2g for GFR less than 30mL/min).

Cephalosporins - Many of have a wide therapeutic window. Suggested guidance: cefepime: 50-100% 12-24 hourly for GFR 10-50mL/min, 25-50% 24-hourly for GFR <10mL/min; cefotaxime: 1g 24-hourly for GFR <10mL/min; ceftazidime: 1g 12-24 hourly for GFR 16-30mL/min, 0.5-1g 24-hourly for GFR<15mL/min; cefuroxime: 500mg 24-hourly for GFR <10mL/min; cephazolin: 0.5-1g 6-8 hourly for GFR 20-40mL/min, 12-24 hourly for GFR <20mL/min; cephalexin: 100% 8-12 hourly for GFR <10mL/min

Fluoroquinolones - Ciprofloxacin: 50-75% 12-hourly for GFR 10-50mL/min, 50% 12-hourly for GFR<10ml/min (or 100% 24-hourly); norfloxacin: 100% 12-24 hourly for GFR 10-50mL/min, 24-hourly for GFR<10mL/min

Macrolides - Erythromycin: 50-75% at normal dosing interval for GFR<10mL/min; Clarithromycin: 50% 12-hourly for GFR <30mL/min

Miscellaneous - Nitrofurantoin: avoid if GFR <60mL/min; teicoplanin: 100% every 48hr for GFR 10-50mL/min, every 72hr for GFR <10mL/min; trimethoprim: if unavoidable in GFR <15mL/min, use 150mg/day; trimethoprim with sulfamethoxazole: usually normal dosing interval for three days then once-daily, for GFR < 25mL/min Meropenem: 100% 12-hourly for GFR 26-50mL/min, 50% 12-hourly for GFR 10-25mL/min, 50% 24-hourly for GFR<10mL/min.

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FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@rgh.sa.gov.au
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