Duke University Hospital Recommendations for Antimicrobial Dose Adjustments in Adults

POLICY

The protocol promotes the timely verification and administration of optimal antimicrobial dosing.

Background: This clinical protocol provides dose adjustments for adults receiving antimicrobial agents based upon estimated renal function, patient weight and/or indication of the antimicrobial agent in question. These medications were chosen based on their high volume of use, complicated dosing regimens, or past reports of adverse drug reactions when not adjusted for renal function. These dosing regimens are intended to establish and maintain therapeutic dosing concentrations, while avoiding excessive accumulation of the drug or its metabolites and minimizing toxicity.

This clinical protocol must be used in conjunction with clinical evaluation, and adjustments must be made to account for patient-specific characteristics. Factors to consider include age, body weight, drug interactions, hepatic insufficiency, and other concurrent disease states. The severity, type and site of infection, host immunocompetency, as well as the results of culture and susceptibilities influence administration of antimicrobials. This is not a comprehensive list of renally eliminated drugs, merely drugs that are frequently used or are difficult to dose.

Dose modifications are based upon creatinine clearance (CrCl), which can be measured directly or estimated with the following equation:

$$\text{CrCl (ml/min)} = \frac{140 - \text{age}}{\text{SCr}} \quad (\times .85 \text{ if female})$$

**Situations when SCr may not be predictive of CrCl: malnutrition/cachexia, liver disease, paralysis, bed-ridden, tacrolimus/cyclosporine, hypervolemia. Age >70 may consider correcting SCr to 1.0.

RESPONSIBILITY

Medical staff
Inpatient Pharmacy staff

PROCEDURE

1. The clinical pharmacist is responsible for reviewing each patient's drug therapy for proper dosing based on renal impairment and antimicrobial indication (as appropriate). The pharmacist shall convert the prescribed dose to one consistent with the patient's renal function as outlined in Appendix A. Doses may be adjusted up or down based on patient's renal function. Doses may be adjusted based on indication as outlined in Appendix B. Surgical prophylaxis dose adjustments may be made according to Appendix C.
    a. Changes may be made in Epic as "Per protocol, no cosign required," and providers will be notified of dose adjustment via page or verbal communication
    b. Document change via I-vent (e.g. Antimicrobial Stewardship, Dose Change or Pharmacotherapy Intervention, Renal Adjustment)

2. The dose conversion may be overridden, at any time, by the prescriber writing "Dose as Written" or other equivalent orders with the medication order
3. This procedure does not apply to the first dose of a medication if a SCr is not immediately available
4. Pharmacists may order a SCr based on "Laboratory Test Ordering by Clinical Pharmacists"
5. If a medication is not listed in the following charts, the prescriber must be contacted directly and a verbal order must be obtained before any dose adjustment can be made.

APPENDICES

Appendix A: Renal Dose Adjustment Table

Drug	Usual Dose	eGFR (mL/min)	Adjusted Dose
Acyclovir IV (use IBW)	HSV: 5 mg/kg q8h HSV encephalitis/zoster: 10 mg/kg q8h	25-49, CRRT	Same dose q12h
		10-24	Same dose q24h
		<10, IHD†, PD	HSV: 2.5 mg/kg q24h HSV encephalitis/zoster: 5 mg/kg q24h
Amikacin	Pharmacist to dose per PK policy		
Amoxicillin	250mg-1gm q8h-q12h	Do not use 875mg dose if CrCl <30	
		10-29	500mg q12h
		<10, IHD†	500mg q24h
Amoxicillin-clavulanate	250mg-500mg q8-12hr or 875mg q12h	Do not use 875mg dose if CrCl <30	
		10-29	500mg q12h
		<10, IHD†	500mg q24h
Ampicillin IV	1g-2g q4-8h	10-50, CRRT	If original q4h dose, q6-8h If original q6h dose, q8-12h
		<10, IHD	Q12h
Ampicillin-sulbactam	1.5g-3g q6h	15-29	Same dose q12h
		<15, IHD†	Same dose q24h
		CRRT	Same dose q8h
Aztreonam	1-2g q8h	10-29	50% of dose q8h
		<10, IHD†	Same dose q24h
		CRRT	Same dose q12h
Cefazolin	2g q8h	10-29, CRRT	1g q12h
		IHD†	1g q24h or 2g/2g/3g with dialysis
Cephalexin	500mg q6h	10-49	500mg q8h
		<10, IHD	500mg q12h
Cefdinir	300mg q12h	<30	300mg q24h
		IHD	300mg q48h and 300mg at the end of each HD session
Cefepime	See Alternative Dosing Substitution of Cefepime protocol for detailed dosing information		

Ceftaroline	600mg q12h Complicated MRSA: 600mg q8h	31-50	400mg q12h Complicated MRSA: 400mg q8h
		15-30	300mg q12h Complicated MRSA: 300mg q8h
		<15, IHD	200mg q12h Complicated MRSA: 200mg q8h OR 300mg q12h
		CRRT	400mg q12h Complicated MRSA: 400mg q8h
Ceftazidime	2g q8h	10-50	2g q12h
		<10, IHD†	2g q24h OR 2g/2g/2g three times per week post IHD
		CRRT	2g q12h
Ceftazidime-avibactam	2.5g q8h	31-50	1.25g q8h
		16-30	0.94g q12h
		6-15	0.94g q24h
		</=5, IHD†	0.94g q48h
		CRRT	1.25g q8h
Ceftolozane-tazobactam	1.5-3g q8h	30-50	750mg-1.5g q8h
		15-29	375mg-750mg q8h
		<15, IHD	750mg-1.5g loading dose, then 150mg-375mg q8h
		CRRT	750mg-1.5g q8h
Cefuroxime PO	250mg-500mg q12h	10-29	250mg-500mg q24h
		<10, IHD†	250mg-500mg q48h
Ciprofloxacin IV	400mg q12h *Pseudomonas*: 400mg q8h	10-29	400mg q24h *Pseudomonas*: 400mg q12h
		<10, IHD†	200-400mg q24h *Pseudomonas*: 400mg q24h
		CRRT	400mg q12h *Pseudomonas*: 400mg q12h
Ciprofloxacin PO	500mg q12h *Pseudomonas* or osteo: 750mg q12h	10-29	500mg q24h *Pseudomonas*: 750mg q24h
		<10, IHD†	500mg q24h *Pseudomonas*: 500mg q24h
		CRRT	500mg q12h *Pseudomonas*: 750mg q12h
Daptomycin	6-12 mg/kg q24h	<30	Q48h
		IHD†	Contact Infectious Diseases MD: either q48h

			or post-HD may be utilized
		CRRT	Q48h
Ertapenem	1g q24h	<30, IHD†	500mg q24h
Fluconazole	100mg-400mg q24h	<50, CRRT, IHD†	Usual loading dose, then 50% of dose q24h
Gentamicin	Pharmacist to dose per PK policy		
Levofloxacin IV and PO	500mg q24h *Pseudomonas*, LRTI or complicated UTI: 750mg q24h	20-49	500mg loading dose, then 250mg q24h *Pseudomonas*, LRTI or complicated UTI: 750mg q48h
		<20, IHD†	500mg loading dose, then 250mg q48h *Pseudomonas*, LRTI or complicated UTI: 750mg loading dose, then 500mg q48h
		CRRT	500mg loading dose, then 250mg q24h *Pseudomonas*, LRTI or complicated UTI: 750mg loading dose, then 500-750mg q24h
Imipenem	Mycobacterium: 500mg q6h GNR – Moderate infection: 500mg q6h GNR – Severe infection: 1000mg q6h	40-70	Mycobacterium: 500mg q8h GNR – Moderate infection: 500mg q8h GNR – Severe infection: 750mg q8h
		21-40	Mycobacterium: 250mg q6h GNR – Moderate infection: 250mg q6h GNR – Severe infection: 500mg q6h
		<20, IHD	Mycobacterium: 250mg q12h GNR – Moderate infection: 250mg q12h GNR – Severe infection: 500mg q12h
		CRRT	Mycobacterium: 250mg q6h GNR – Moderate infection: 250mg q6h GNR – Severe infection: 500mg q6h
Meropenem	See Alternative Dosing Substitution of Meropenem protocol detailed dosing information		
Meropenem-vaborbactam	4g q8h	30-49	2g q8h
		15-29	2g q12h
		<15, IHD	1g q12h
Oseltamivir	Treatment: 75mg q12h	30-59	30mg q12h
		10-30	30mg q24h
		IHD	30mg after every HD cycle
		PD	A single 30mg dose administered immediately after a dialysis exchange
Piperacillin-tazobactam	3.375g-4.5g q8h Extended Infusion **(4-hrs)**	<20, IHD	3.375g-4.5g q12h
		CRRT	3.375g-4.5g q8h
TMP/SMX	UTIs or cellulitis: 1-2 DS tab q12h	10-30, IHD†	UTIs or cellulitis: 1-2 DS tab q24h PCP or serious systemic infections: 5

	PCP or serious systemic infections: 5mg/kg q6-8h		mg/kg/dose q8h
		CRRT	UTIs or cellulitis: 1-2 DS tab q12h PCP or serious systemic infections: 5-7.5mg/kg/dose q12h
Tobramycin	Pharmacist to dose per PK policy		
Vancomycin	Pharmacist to dose per PK policy		

†If patient is on hemodialysis (IHD) schedule administration so that patient received daily dose immediately **after** dialysis.

Appendix B: Indication Dose Adjustment Table

Drug	Indication	Dose Adjustment
Ceftriaxone	CAP, UTI	Pharmacist may adjust dose regimen to 1g q24h
Cefepime	Pharmacist may adjust from extended infusion to traditional infusion and vice versa based on indication as outlined in the "Alternative Dosing Substitution of Cefepime" protocol	
Clindamycin IV	Non-CNS toxoplasmosis	Pharmacist may adjust 600mg q6h to 600mg q8h Contact MD if need to increase dose to 900 mg q8h for necrotizing fasciitis
Meropenem	Pharmacist may adjust from extended infusion to traditional infusion and vice versa based on indication as outlined in the "Alternative Dosing Substitution of Meropenem" protocol	
Metronidazole	Non-CNS infection	Pharmacist may adjust 500mg q6h to 500mg q8h

Appendix C. Pre-operative Antibiotic Dose Adjustment Policy

Drug	Dose (one-time doses only)
Ampicillin-sulbactam	3g
Cefazolin	2g if weight <120kg, 3g if weight >=120kg
Ciprofloxacin	400mg
Clindamycin	900mg
Doxycycline	100mg
Ertapenem	1g
Gentamicin *For obese patients (greater than 25% over IBW), gentamicin should be dosed using adjusted BW where ABW=[0.4x(TBW-IBW)+IBW]	5mg/kg if CrCl >30; 1.5mg/kg if CrCl <30
Metronidazole	500mg
Vancomycin*	1g if <80kg, 1.5g if 80-119kg, 2g if >/=120 kg

***Exception: CT Surgery uses pre-op vancomycin doses at 20mg/kg**