Adapted from: Heintz BH, Matzke GR, Dager WE. Antimicrobial Dosing Concepts and Recommendation for Critically Ill Patients Receiving Continuous Renal Replacement Therapy or Intermittent Hemodialysis. Pharmacotherapy 2009;29(5) 562-577.

Recommended Adult Antimicrobial Dosage by Type of Renal Replacement Therapy

Antimicrobial[a]	**Loading Dose for CRRT**	**Maintenance Dose for CRRT**			
		(CVVH)[b,c]	**CVVHD**[b]	**CVVHDF**[b]	**IHD**[d]
Acyclovir[8,51,53,54]	none	5-10 mg/kg q24h[e]	5-10 mg/kg q12-24h[e]	5-10 mg/kg q12-24h[e]	2.5-5 mg/kg q24h[e]
Amikacin[8,51,53,54]	10 mg/kg	7.5 mg/kg q24-48h[f]	same	same	5-7.5 mg/kg q48-72h[g]
Amphotericin B Deoxycholate[42,51,53,54]	none	0.5-1 mg/kg q24h	same	same	same
Amphotericin B Liposomal[42,51,53,54]	none	3-5 mg/kg q24h	same	same	same
Ampicillin[8,51]	2 g	1-2 g q 8-12h	1-2 g q8h	1-2 g q 6-8h	1-2 g q12-24h
Ampicillin-sulbactam[8,51,53]	3 g	1.5-3 g q8-12h	1.5-3 g q8h	1.5-3 g q 6-8h	1.5-3 g q12-24h
Azithromycin[8,51,54]	none	250-500 mg q24 h	same	same	same
Aztreonam[51,53,54,59]	2 g	1-2 g q12h	1 g q8h or 2 g q12h[h]	1 g q8h or 2 g q12h[h]	500 mg 12h
Caspofungin[51,54]	70mg	50mg q24h	same	same	same
Cefazolin[8,51,53,54,59]	2 g	1-2 g q12h	1 g q8h or 2 g q12[h]	1 g q8h or 2 g q12h[h]	500-1000 mg q24h[i]
Cefepime[8,42,51,53,54,60,61]	2 g	1-2 g q12h	1 g q8h or 2 g q12h[h,j]	1 g q8h or 2 g q12h[h,j]	500-1000 mg q24h[i]
Cefotaxime[8,42,51-53,59]	none	1-2 g q8-12h	1-2 g q8h	1-2 g q6-8h	1-2 g q24h
Ceftazidime[8,42,51-54,62]	2 g	1-2 g q 12h	1 g q8h or 2 g q12h[h,j]	1 g q8h or 2 g q12h[h,j,k]	500-1000 mg q24h[i]
Ceftriaxone[8,42,51,53,54]	2 g	1-2 g q12-24h	same	same	1-2 g q24h
Ciprofloxacin[8,42,51,53,54]	none	200-400 mg q12-24h	400 mg q12-24h	400 mg q12h	200-400 mg q24h
Clindamycin[8,51,53,54]	none	600-900 mg q8h	same	same	same
Colistin[42,51,53,63]	none	2.5 mg/kg q48h[l]	2.5 mg/kg q24-48h[l]	2.5 mg/kg q12-24h[l,m]	1.5 mg/kg q24-48h
Daptomycin[51,53,54,64,65]	none	4-6 mg/kg q24 -48h[n]	4-6 mg/kg q24 -48h[n]	4 – 6mg/kg q24h 8-10mg/kg q48h	4-6 mg/kg q48-72, post-HD only[n]
Doxycycline[51,52,54]	none	100 mg q12h	same	same	same
Ertapenem[8,51,53,54]	none	1000 mg q24h	same	same	500mg q24h[o]
Fluconazole[8,51-54,66,67]	400-800 mg	200-400 mg q24h	400-800 mg q24h[p]	800 mg q24h[q]	200-400 mg q48h or 100-200 mg q24h
Ganciclovir[8,42,51] (CMV infection)	none	I = 2.5 mg/kg q24h M = 1.25 mg/kg q24h	I = 2.5 mg/kg q 12h M = 2.5mg/kg q24h	I = 2.5 mg/kg q 12h M = 2.5mg/kg q24h	I = 1.25 mg/kg q48-72h M = 0.625mg/kg q48-72h
Gentamicin[47,51,54,68]	2-3 mg/kg				2-3 mg/kg load x 1, then
Mild UTI / Synergy (gent):		1 mg/kg q24-36h (redose when Cp < 1mg/L)			1 mg/kg q48-72h[r]
Moderate-Severe UTI:		1-1.5 mg/kg q24-36h (redose when Cp < 1.5-2mg/L)			1-1.5 mg/kg q48-72h[r]
Systemic GNR infection:		1.5-2.5 mg/kg q24-48h (redose when Cp < 3-5mg/L)			1.5-2 mg/kg q48-72h[r]

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Antimicrobial[a]	Loading Dose for CRRT	Maintenance Dose for CRRT (CVVH)[b,c]	CVVHD[b]	CVVHDF[b]	IHD[d]
Imipenem[8,27,37,42,51,53,54,69]	1 g	500 mg q8h[s]	500 mg q6-8h[s]	500 mg q6h[s]	250-500 mg q12h
Itraconazole[42,51,52,54]	none	200 mg q12h x 4 doses, then 200mg q24h	same	same	same
Levofloxacin[42,51-54]	500-750 mg	250mg q24h	250-500 mg q24h	250-750 mg q24h	250-500 mg q48h
Linezolid[42,51-54]	none	600 mg q12h	same	same	same
Meropenem[28,29,42,51-54,70-73]	1 g	0.5-1g q12h[t]	0.5-1g q8-12h[t]	0.5-1g q8h[t,u]	500 mg q24h
Metronidazole[51,54]	none	500 mg q6-12h[v]	same	same	500 mg q8-12h[v]
Micafungin[51,54]	none	100-150 mg q24h (treatment); 50 mg q24h (prophylaxis)			same
Moxifloxacin[42,51,53,54]	none	400 mg q24h	same	same	same
Nafcillin[51,53,54]	none	2 g q4-6h	same	same	same
Penicillin G[8,51,54]	4 MU	2 MU q4-6h	2-3 MU q4-6h	2-4 MU q4-6h	normal dose load x 1, then 25-50% normal dose q4-6h or 50-100% normal dose q8-12h[w]
Piperacillin-Tazobactam[25,51,54]	none	2.25-3.375 g q6-8h	3.375 g q6h	3.375 g q6h	2.25 g q8-12h
Rifampin[51,54]	none	300-600 mg q12-24h[v]	same	same	same
Ticarcillin-Clavulanate[51,53,54]	3.1 g	2 g q6-8h	3.1 g q6-8h	3.1 g q6h	2 g q12h[x]
Tigecycline[51,54]	100 mg	50 mg q12h	same	same	same
Tobramycin[47,51,54,68]	2-3 mg/kg	GNR infection: 1.5-2.5 mg/kg q24-48h (see gentamicin for redosing)			Same as gentamicin
TMP-SMX[51]	none	2.5-7.5 mg/kg (TMP) q12h[v]	same	same[y]	2.5-10 mg/kg (TMP) q24h[v] or 5-20 mg/kg TIW post HD[v]
Vancomycin[42,46,51-54,70,74-78]	15-25 mg/kg	10-15mg/kg q24-48h[z,aa,bb]	10-15 mg/kg q24h[z,aa,cc]	7.5-10 mg/kg q12h[z,aa]	Load 15-25 mg/kg on day 1, then give 5-10 mg/kg after HD[z,dd]
Voriconazole[42,51-54]	400 mg po q12h x 2	200mg po q12h[ee]	same	same	same

CRRT = continuous renal replacement therapy; CVVH = continuous venovenous hemofiltration; CVVHD = continuous venovenous hemodialysis; CVVHDF = continuous venovenous hemodialfiltration; EDD = extended daily dialysis; GFR = glomerular filtration rate; IHD = intermittent hemodialysis; HD = hemodialysis; Cp = plasma drug concentration(s); CMV = cytomegalovirus; I = induction dosing; M = maintenance dosing; gent = gentamicin; TIW = three times weekly; GNR = Gram-negative rods, GPC = Gram-positive cocci, MU = million units

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a. Doses are based on the provided references and/or the authors' opinion, especially when available references are limited or outdated, however should not replace clinical judgment.

b. All CRRT doses assume ultrafiltration and dialysis flow rates of 1-2 L/h, intravenous administration and minimal residual renal function. Dosing ranges are provided to accommodate for differences in ultrafiltration and dialysis flow rates, patient size, severity and site of infection, MIC of infecting pathogen(s), level of intrinsic renal function and immune status, among other factors.

c. Scheetz MH et al.,[59] note that clearance of antimicrobials by CVVH depends on the CVVH filtration rate, primarily for antimicrobials with low PBC and Vd and provide dosing recommendations for aztreonam, cefazolin, cefotaxime, ceftazidime, imipenem and piperacillin for CVVH filtration rates of 1-4 L/h.

d. Hemodialysis assumes a TIW regimen and the patient received the full dialysis session (use clinical judgment); administer *after* dialysis for q24-72h dosing; doses assume critically ill patients with serious infections receiving standard IHD; extended daily dialysis (EDD) may require larger doses than standard IHD.

e. Use higher end of dosing range for viral meningoencephalitis and Varicella zoster virus infections (e.g. 10 mg/kg q12 among patients receiving CVVHDF).

f. For severe GNR infections target peak = 15-30mg/L; redose when Cp < 10mg/L.

g. Redose when pre-HD levels (Cp) < 10mg/L; redose when post-HD levels (Cp) < 6-8mg/L.

h. Doses of 1 g IV q8h results in similar steady state Cp as 2 g IV q12h, however is more cost-effective.

i. Administer after dialysis on dialysis days; as an alternative, dose 1-2 g IV q48-72h post-dialysis.

j. Doses of 2 g IV q8h may be needed for GNR pathogens with an MIC ≥ 4mg/L.

k. Mariat C et al.,[62] recommend dosing ceftazidime 3 g IV as a continuous infusion over 24h after 2 g load to maintain Cp ≥ 4 x MIC for all susceptible pathogens in CVVHDF.

l. Drug clearance is highly dependent on the method of renal replacement, filter type, flow rate, site of infection, MIC of infecting pathogen(s), etc. For example, 2.5 mg/kg IV q24h may be required in patients receiving CVVHD with deep-seated infections and/or highly resistant GNR pathogens. Appropriate dosing requires close monitoring of pharmacologic response, signs of adverse reactions due to drug accumulation, as well as drug levels in relation to target trough (if appropriate).

m. Li J et al.,[63] recommend dosing colistin up to 2.5 mg/kg IV q12 h in patients receiving CVVHDF to achieve adequate Cp for highly resistant GNR pathogens.

n. Churchwell M et al.,[64] Burkhardt O et al.[65] / Kielstein JT (ICAAC 2001) note that dosing daptomycin 4-6 mg/kg IV q48h in CRRT and EDD, respectively, may result in significant underdosing and recommend daily dosing. Consider dosing 4-6 mg/kg IV q24h (or 8 mg/kg IV q48h) for critically ill patients receiving CRRT with deep-seated infections or those not responding to standard dosing. Therapeutic drug monitoring and/or more frequent creatine kinase serum levels may be warranted if dosing is increased. Patel N et al recommend increasing the dose by 50% for a 72 hour dosing interval (e.g. for Friday's dose of a MoWeFri regimen give 9mg/kg vs. 6mg/kg).

o. Burkhardt O, et al recommend dosing ertapenem 1000 mg IV q24h in EDD.

p. Bergner R et al.,[66] recommend dosing fluconazole 800 mg IV/PO q24h in CVVHD if the dialysate flow rate is ≥ 2 L/h and/or treating fungi with relative triazole resistance (e.g. *Candida glabrata*).

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q. Yagasaki K et al.,[67] recommend dosing fluconazole 500-600 mg IV q12h in CVVHDF.

r. Need for gentamicin redosing is primarily dependent on the clinical indication and availability of gentamicin levels (Cp), including reported values and timing (e.g. pre vs. post-HD). Consider redosing gentamicin for pre-HD levels < 1mg/L (mild UTI and synergy), < 1.5-2mg/L (moderate-severe UTI) and < 3-5mg/L (severe GNR infection). Consider redosing gentamicin for post-HD levels < 1mg/L (UTI and synergy) and < 2mg/L (severe GNR infection).

s. Fish D et al.,[69] note imipenem doses of 500 mg IV q8-12h appear to achieve adequate Cp needed to treat most GNR pathogens with MIC ≤ 2mg/L in patients receiving CRRT, however they recommend dosing imipenem 500 mg IV q6h to achieve adequate target attainment for pathogens with MIC = 4-8mg/L or for deep-seated infections in patients receiving CRRT.

t. Consider dosing meropenem 500 mg q8h or 1 g q12h in CVVH and 500 mg q6-8h or 1 g q8-12h in CVVHD(F).

u. Robatel C et al.,[73] recommend to dose meropenem 750 mg IV q8h or 1500 mg IV q12h in CVVHDF to optimize pharmacodynamic target attainment.

v. Dosing regimen is highly dependent on clinical indication (e.g. Trichomoniasis vs. *Clostridium difficile* colitis for metronidazole; tuberculosis vs. infective endocarditis for rifampin; and cystitis vs. *Pneumocystis jiroveci* pneumonia for TMP-SMX). Consider 10mg/kg IV daily in EDD.

w. Mild-moderate infections: 0.5-1 MU IV q4-6h or 1-2 MU IV q8-12h; neurosyphilis, endocarditis or serious infections: doses up to 2 million units IV q4-6h; administer after HD on days of dialysis or supplement with 500,000 units after dialysis.

x. A supplemental dose of 3.1 g is recommended post-dialysis. As an alternative, consider dosing 2 g IV q8h without a supplemental dose for deep-seated infections.

y. Doses up to 10mg/kg IV q12h may be required for critically ill patients with *Pneumocystis jiroveci* pneumonia receiving CVVHDF.

z. Recommended vancomycin doses and need for redosing needs to be individualized as they are dependent on a number of variables, including reported and targeted vancomycin concentrations (see text).

aa. Consider redosing vancomycin for Cp < 10-15 mg/L for CRRT.

bb. Doses of vancomycin typically ranges from 500-1500 mg IV q24-48h among patients receiving CVVH to achieve desired Cp; however doses may need to be increased to achieve target vancomycin Cp of 15-20mg/L (e.g. *Staphylococcus aureus* deep-seated infections).

cc. 7.5 mg/kg IV q12h may be required among patients receiving CVVHD to achieve desired Cp.

dd. Consider redosing vancomycin for pre-HD Cp as follows: < 10mg/L – give 1000 mg after HD, 10-25mg/L – give 500-750 mg after HD, > 25mg/L – hold vancomycin. Consider redosing vancomycin 500-1000 mg for post-HD Cp < 10-15mg/L; however recommended doses and need for redosing are dependent on reported and targeted vancomycin concentrations, utilization of high vs. low-flux filters, among other factors (see text).

ee. Oral therapy preferred to prevent accumulation of cyclodextran vehicle; bioavailability > 95%.

Approved by UCDH Pharmacy & Therapeutics Committee 12/2017.