Maine Medical Center
MaineHealth

Adult Antimicrobial Formulary Guide

Updated: 2010

Adult Antimicrobial
Stewardship Program (ASP)

Department of Pharmacy Services
& Division of Infectious Diseases

Adult Antimicrobial Stewardship Program (ASP)

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Approved by the Executive Committee and the Pharmacy & Therapeutics Committee.

Antimicrobial Formulary Guide 2010

Contents

Disclaimer

This Formulary Guide is published by the Antimicrobial Decision Support Program and is intended as a general reference principally to clinicians practicing at MMC. The information has been summarized and does not constitute medical advice. Medical advice must be customized to specific circumstances of each individual patient, and because this information changes rapidly, nothing provided in this handbook should be used as a substitute for medical advice. Readers are encouraged to consult with several resources to determine appropriate patient treatment. The authors have used sources believed to be reliable in compiling the information contained in this Formulary Guide.

Organisms & Suggested Definitive Treatment Regimens*

Staphylococcus aureus

IV:		PO:	
1. Oxacillin	$$$$	1. Dicloxacillin	$
2. Cefazolin	$	2. Cephalexin	$
3. Doxycycline	$	3. TMP-SMX	$
4. TMP-SMX	$$$	4. Clindamycin	$
5. Clindamycin	$$	5. Doxycycline	$
6. Vancomycin (MRSA) [G]	$$	6. Minocycline	$
7. Linezolid (MRSA) ®	$$$$$$	7. Linezolid (MRSA) ®	$$$$$

Coagulase Negative Staphylococcus

IV:

1. Vancomycin [G] $$
2. *Other choices may be available depending on the INFX/susceptibility results*

Enterococcus faecalis *- Predominate enterococcus spp., accounting for approximately 85% of all isolates. Typically 100% susceptible to penicillin's.*

IV:†		PO:	
1. Ampicillin	$$	1. Amoxicillin	$
2. Vancomycin	$$	2. Nitrofurantoin (UTI only)	$
3. Piperacillin/Tazo & Doripenem both active if treating mixed INFXs		3. +/- Doxycycline	$

Enterococcus faecium- *Accounts for ~15% of isolates. Typically 30% susceptible to vancomycin.*

IV: †		PO:	
1. Linezolid (VRE) ®	$$$$$	1. Linezolid (VRE) ®	$$$$$
2. Daptomycin (VRE) ®	$$$$$$	2. +/- Doxycycline	$
3. +/- Vancomycin	$$	3. +/- Nitrofurantoin (UTI only)	$

† *IF endocarditis or bloodstream INFX: Add gentamicin or streptomycin*

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* *Based on MMC in-vitro susceptibility report* ® *Formulary Restriction*

$ - $$$$$$ = Least expensive - most expensive

Non-Enterococcal Streptococci

IV:		PO:	
1. Penicillin G	$	1. Penicillin VK	$
2. Cefazolin, Ceftriaxone	$	2. Cephalexin, Cefdinir	$
3. Clindamycin	$$	3. Clindamycin	$
4. Azithromycin	$$	4. Azithromycin	$
5. Vancomycin [G]	$$		

Streptococcus pneumoniae

[Penicillin Susceptible (MIC ≤ 2 mcg/mL) & Non-CNS infection]

IV:		PO:	
1. PCN$		1. PCN	$
2. Ampicillin	$	2. Amoxicillin	$
3. Vancomycin (PCN Allergic)	$$	3. Doxycycline (PCN Allergic)	$

Streptococcus pneumoniae

[Intermediately Penicillin Resistant (MIC = 4 mcg/mL) & Non-CNS infection]

IV:		PO:	
1. Ampicillin/PCN *(High-dose)*	$	1. Amoxicillin (*1g Q8h)*	$
2. Ceftriaxone	$	2. Cefdinir	$
3. Moxifloxacin	$$	3. Moxifloxacin	$$

Streptococcus pneumoniae

[Highly Penicillin Resistant (MIC ≥ 8 mcg/mL) and Non-CNS Infection]

IV:		PO:	
1. Moxifloxacin	$$	1. Moxifloxacin	$$
2. Ceftriaxone (MIC< 4 mcg/mL)	$		
3. Vancomycin	$$		

Streptococcus pneumoniae

(Highly Penicillin Resistant Strains)

Meningitis

IV:

1. Ceftriaxone +	$
Vancomycin	$$

[G] See Dosing and Formulary Guidelines/Clinical Pearls section (pages 14-19)

Organisms & Suggested Definitive Treatment Regimens cont'd*

Haemophilus Influenzae

IV:		PO:	
1. Ceftriaxone	$	1. Amoxicillin/Clavulanate	$
2. Doxycycline	$	2. Cefdinir	$
3. TMP-SMX	$$$	3. TMP-SMX	$
		4. Doxycycline	$

Legionella

IV:

1. Moxifloxacin	$$
2. Azithromycin +/- Rifampin	$ +/- $$$

Bacteroides Fragilis

IV:		PO:	
1. Metronidazole	$	1. Metronidazole	$
2. Ampicillin/Sulbactam	$$	2. Moxifloxacin	$$
3. Moxifloxacin	$$	3. Amoxicillin/Clavulanate	$
5. Piperacillin/Tazobactam☆	$$$$		
6. Doripenem☆	$$$$-$$$$$		

☆ P*olymicrobial infections only*

Gram (-) Aerobic Organisms (Enterobacteriaceae)

IV:		PO:	
1. Aminoglycosides [AMGs]	$	1. Ciprofloxacin/	$
a. Gentamicin		Moxifloxacin	$$
b. Tobramycin		2. Cefdinir	$
2. Cefepime	$$	3. TMP-SMX	$
3. Ciprofloxacin,	$		
Moxifloxacin	$$		
4. TMP/SMX	$$$		
5. Piperacillin/Tazobactam	$$$$		
6. Doripenem	$$$$-$$$$$		

***** *Based on MMC in-vitro susceptibility reports* *® Formulary Restriction*

[G] See Dosing and Formulary Guidelines/Clinical Pearls (pages 9-18)

Pseudomonas aeruginosa

IV:

1. Gentamicin/Tobramycin + Cefepime	$$$
2. Gentamicin/Tobramycin + Piperacillin/Tazobactam	$$$$$
3. Gentamicin/Tobramycin + Doripenem	$$$$-$$$$$
4. Ciprofloxacin as an alternative to an AMG in pts. at high risk for nephrotoxicity**	$$$-$$$$$
5. Aztreonam as an alternative to B-lactams in pts. with documented type I, IgE allergy	$$$$$-$$$$$$
6. Amikacin in place of other AMG's for resistant organisms only [G]	$$$-$$$$$

***Quinolones are NOT synergistic when combined with AMGs (Neu H. Drugs 1993;45: 54-58.)*

Clostridium difficile Infection

1st/2nd Episode – Mild to Moderate C. diff

1. Metronidazole 500mg **PO** Q8h x 10-14d	$

1st/2nd Episode – Severe C. diff✦

1. Vancomycin 125mg **PO** Q6h x 10-14d	$$

Illeus/Toxic Megacolon✦

1. Metronidazole 500mg **IV** Q6h x 10-14d	$$
+/- Vancomycin **PO** 125mg Q6h (if possible)	
+/- Intracolonic Vancomycin 500mg in 100mL NS per rectum Q6h as a retention enema	$$$

> 3rd Recurrence

1. Vancomycin 125mg **PO** Q6h x 10-14d	$$

- Followed by *Pulse therapy* → 125mg PO every 2-3days x 2-8weeks

Refractory Disease:

- Consider *GI* consultation for evaluation of donor stool transplant

+/- Rifampin 300mg PO Q12h (if *no improvement after 4 days of monotherapy)*

✦ *Consider gastroenterology & surgery consultation*

Cohen SH, et al. *Infect Control Hosp Epi* 2010; 31(5):431-455.

MMC Formulary: Oral Antimicrobials

Drug	Usual Regimen*	$ Cost/Day**
Penicillins		
Amoxicillin	500mg Q8h	0.53
Amoxicillin/Clavulanate	875mg/125mg Q12h	1.51
Dicloxacillin	500mg Q6h	1.68
Penicillin VK	500mg Q6h	0.56
Cephalosporins		
Cephalexin	500mg Q6h	0.32
Cefdinir	300mg Q12h	2.60
Fluoroquinolones		
Ciprofloxacin	500mg-750mg Q12h	0.28-0.44
Moxifloxacin	400mg Q24h	10.22
Macrolides/Azalides		
Azithromycin	250mg-500mg Q24h	1.11-2.22
Clarithromycin	250mg-500mg Q12h	0.56-0.60
Erythromycin	500mg Q6h	1.48
Miscellaneous		
Clindamycin	150mg-300mg Q8h	1.00-2.00
Doxycycline	100mg Q12h	0.14
Metronidazole	500mg Q12h-8h	0.10-0.15
Minocycline	200mg Qhs	0.48
Nitrofurantoin IR [G]	100mg Q6h	2.76
Linezolid ®	600mg Q12h	140.36
TMP/SMX [G]	160mg/800mg Q12h	0.12
Vancomycin [G]	125mg Q6h	2.42
Antifungals		
Clotrimazole troche	10mg 5x daily	4.11
Fluconazole [G]	200mg-400mg Q24h	0.18-0.35
Voriconazole [G]	100mg-200mg Q12h	38.72-77.40
Antivirals		
Acyclovir	200mg 5x day- 400mg Q8h	0.30-0.36
	800mg 5x day	1.12
Famciclovir	500 mg Q8h	19.38
Ganciclovir	1000mg Q8h	34.20
Valacyclovir	0.5g-1g Q8-12h	12.74-38.22
Valganciclovir ®	900mg Q12h-24h	53.58-107.16
Oseltamivir	75mg Q12-24 h	7.82-15.64
Antituberculosis		
Ethambutol	15mg/kg Q24h	1.80
Isoniazid	300mg Q24h	0.06
Pyrazinamide	1.5-2g Q24h	1.89-2.42
Rifampin	600mg Q24h	0.44

Usual PO Adult Dose: based on an adult **(70kg) patient with normal renal function*

*** Cost is MMC acquisition cost*

MMC Formulary: Parenteral Antimicrobials

Drug	Usual Regimen*	$ Cost/Day**
Penicillins		
Ampicillin	1gm-2g Q6h	13.46-21.73
Ampicillin/Sulbactam	1.5g-3g Q6h	6.85-13.34
Oxacillin	1g-2g Q4-6h	29.44-88.32
Piperacillin/Tazobactam [G]	3.375g-4.5g Q6h	61.55-82.06
Penicillin G	2 – 4 millionU Q4h	8.02-16.04
Cephalosporins		
First Generation		
Cefazolin	1g-2g Q8h	1.87-3.74
Third Generation		
Ceftazidime	1g-2g Q8h	10.88-20.19
Ceftriaxone [G]	1g-2g Q24h	1.20-2.89
Fourth Generation		
Cefepime [G]	1g-2g Q12h	10.54-21.06
Other Beta-lactams		
Aztreonam [G]	1g-2g Q8h	99.81-197.91
Meropenem [G]	1g Q8h	163.70
Doripenem [G]	500mg/1000mg Q8h	75.18-150.36
Aminoglycosides [G]		
Amikacin	Variable (see guidelines)	5.89
Gentamicin	Variable (see guidelines)	3.99-5.70
Tobramycin	Variable (see guidelines)	5.25-6.18
Fluoroquinolones		
Ciprofloxacin	400mg Q12h	3.76
Moxifloxacin	400mg Q24h	11.54
Macrolides/Azalides		
Azithromycin	500mg Q24h	4.42
Erythromycin	500mg Q6h	36.77
Oxazolidinone		
Linezolid ®	600mg Q12h	183.30
Miscellaneous		
Rifampin	600mg Q24h	36.54
Clindamycin	600mg Q8h	8.68
Doxycycline	100mg Q12h	7.89
Metronidazole	500mg Q12h-8h	2.44-3.66
Metropime	500mg/1g Q12h	12.98
(Metronidazole + Cefepime)	500mg/2g Q12h	24.72
TMP/SMX [G]	(variable)[†]	37.10
Vancomycin [G]	1g Q12h	9.68
Daptomycin ®	4mg/kg - 6mg/kg Q24h	119.04-178.56

*[†]Dose based on trimethoprim: PCP dose = 20mg/kg/day ÷ Q6-8h**

Parenteral Antimicrobials cont'd

Drug	Usual Regimen*	$ Cost/Day**
Antifungals		
Abelcet [G]	5mg/kg Q24h	300.00
Amphotericin B	0.6-1mg/kg Q24h	15.00
Fluconazole [G]	200mg-400mg Q24h	6.26-6.71
Voriconazole ®	6mg/kg x 2 doses	478.45
	4mg/kg Q12h (Maintenance)	318.90
Micafungin ®	100mg-150mg Q24h	108.46-162.69
Antivirals		
Acyclovir	5-10mg/kg Q8h	15.38-30.76
Foscarnet	60mg/kg Q8h (Induction)	115.09
	90-120mg/kg/day (Maintenance)	57.55-80.57
Ganciclovir	5 mg/kg Q12h (Induction)	59.05
	5 mg/kg Q24h (Maintenance)	29.53

® *Formulary Restriction* *[G] Formulary Guidelines*

Usual IV Adult Dose: based on an adult **(70kg) patient with normal renal function*

*** Cost is MMC acquisition cost*

Let's Go P.O. – Transitional Antimicrobial Therapy

- The oral route of administration may be preferred in many circumstances:
  - UTIs (including pyelonephritis), respiratory, SSTIs, & Intra-abdominal INFXs
  - INFXs to AVOID in: Meningitis, septic shock, acute osteomyelitis, *Staphylococcal* bacteremia of unknown origin, undrained abscesses, and severe mucositis

Agents with ≥ 90% Bioavailability		
- Moxi/Cipro-floxacin	- Metronidazole	- TMP/SMX
- Doxy/Mino-cycline	- Clindamycin	- Linezolid
- Flu/Vori-conazole	- Cephalexin	- Rifampin

Criteria for Conversion: based on clinical stability & ability to take PO Meds

- **Functional GI tract**
  - Absence of vomiting
  - Absence of recent GI radiation or surgery
  - Receiving other meds enterally (PO, NG, PEG) or at least a full liquid diet

PLUS

- **Clinical Stability x 24 hours** *as defined objectively by:*
  - Oral temperature < 38°C
  - HR < 100 beats/min
  - SBP >90mmHg without vasopressor support
  - RR < 24 breaths/min

Aminoglycoside Dosing Guidelines: Traditional Adult Dosing

1. **Calculate Dosing Weight** - Use ideal body weight (kg), unless obese (>20% over IBW) in which case use adjusted body weight (AdjBW)

   Ideal Body Weight (IBW)

   - Male: 50 kg + (2.3 x inches of height > 60 inches)
   - Female: 45.5 kg + (2.3 x inches of height > 60 inches)

   Adjusted Body Weight (AdjBW) - *Obese patients*

   - **AdjBW** = IBW + 0.4 (Actual body weight - IBW)

2. **Calculate Initial Dose**- based on **IBW** or **AdjBW**
   - *Round dose to the nearest 50mg increment*

GENTAMICIN (G), TOBRAMYCIN (T), AMIKACIN (A)

Site of Infection	Dose	Goal Peak Concentration
Uncomplicated UTI	**G/T** = 1 - 1.5mg/kg **A** = 3.5 - 4.5mg/kg	
Enterococcal Endocarditis *Synergy w/ cell wall active agent**	**G** = 1 - 1.5mg/kg	G = 3 - 4 mcg/mL
Sepsis and other serious Gm (-) infections	**G/T** = 2 - 2.5mg/kg **A** = 5 - 6mg/kg	
Pneumonia, Acute life threatening infections	**G /T** = 2.5 - 3mg/kg **A** = 7.5mg/kg	

Intraperitoneal administration in CAPD: 4-8mg/L of CAPD fluid

**Cell wall active agents: vancomycin, daptomycin, B-lactams*

3. **Calculate Renal Function** (Cockcroft-Gault equation)

   Calculate Creatinine Clearance (CrCl): Based on IBW or AdjBW, age, and SCr

   Male: $\text{CrCl (ml/min)} = \text{IBW} \frac{(140 - \text{Age})}{72 \times \text{SCr}}$

   Female: **0.85** x CrCl male

   (If SCr < 1 and patient is ≥ 65 years old consider rounding SCr up to 1)

Caution should be exercised when using AMGs in pts. with a CrCl < 30mL/min, and use should be avoided in pts. with CrCl < 20mL/min unless clinically necessary

4. Determine Dosing Interval - based on creatinine clearance

CrCl (mL/min)	Interval
≥ 60	Q 8h *(if patient ≥65 y/o adm. Q 12h)*
40-60	Q 12h
20-40[+]	Q 24h
10-20[+]	Q 48h
< 10	Q 72h
Hemodialysis	1 mg/kg Post-HD
CVVHD	Dose for CrCl 10-20 mL/min
CAPD	Dose for CrCl < 10 mL/min

[+]*Pharmacokinetics consult recommended*

5. Monitoring of Aminoglycoside Levels

Goal Trough Concentrations:

Gentamicin/Tobramycin: < 2.0 mcg/mL (Ideally ≤ 1 mcg/mL)

Amikacin: < 8.0 mcg/mL

Dosing Interval	Type of Level	When to Draw
Q 8-12h	Peak and Trough[*]	3rd Dose
Q 24-48h	Peak and Trough[*]	After 1st dose/before 2nd dose
Q 72h	Peak and Trough[*]	After 1st dose/before 2nd dose
Hemodialysis	Trough	Prior to dialysis

Subsequent dose adjustments should be based on serum levels

[*]**Peak levels:** Drawn 30minutes *after* the infusion *completed* (30min infusion)

[*]**Trough levels:** Drawn *immediately* preceding the dose

Pharmacokinetic (PK) Service

- Free consultation service is available, and is provided 7 days a week by pharmacy services
- Order consultation via SCM under aminoglycoside or vancomycin ordering screens

Aminoglycoside Dosing Guidelines: Extended Interval Dosing (Once-daily)

- Because aminoglycosides (AMG) have concentration dependent activity, the rate of bacterial killing increases as drug concentration is increased
- Optimizing the AMG peak serum concentration to bacterial MIC ratio (Peak:MIC) to a value of ≥ 10:1 maximizes bacterial killing
- In appropriate populations this dosing strategy reduces the selection and emergence of resistant organisms, while minimizing toxicity

Exclusion Criteria:

- Pregnancy, burns (>20% BSA), ascites, dialysis patients, renal failure, enterococcal endocarditis, pediatrics (nomogram based on adult patients), cystic fibrosis (higher doses required ~10-14mg/kg)

Dosing Guidelines:

1. **Calculate Dosing Weight** - See traditional aminoglycoside dosing (page 9)
   - Based on **IBW** (use **AdjBW** if obese)
   - *Round dose to the nearest 50mg increment*

	Dose
Gentamicin/Tobramycin	5-7mg/kg
Amikacin	15-20mg/kg

2. **Initial Dosing Interval** - based on Creatinine Clearance (CrCl)

	CrCl (mL/min)	Dose & Interval
Gentamicin / Tobramycin	≥ 50 mL/min	5-7 mg/kg/24h
	30-49 ml/min[+]	5-7 mg/kg/36h
	≤ 29 ml/min	Avoid use
Amikacin	≥ 40 ml/min	15-20 mg/kg/24h
	30-39 ml/min[+]	15-20 mg/kg/36h
	≤ 29 ml/min	Avoid use

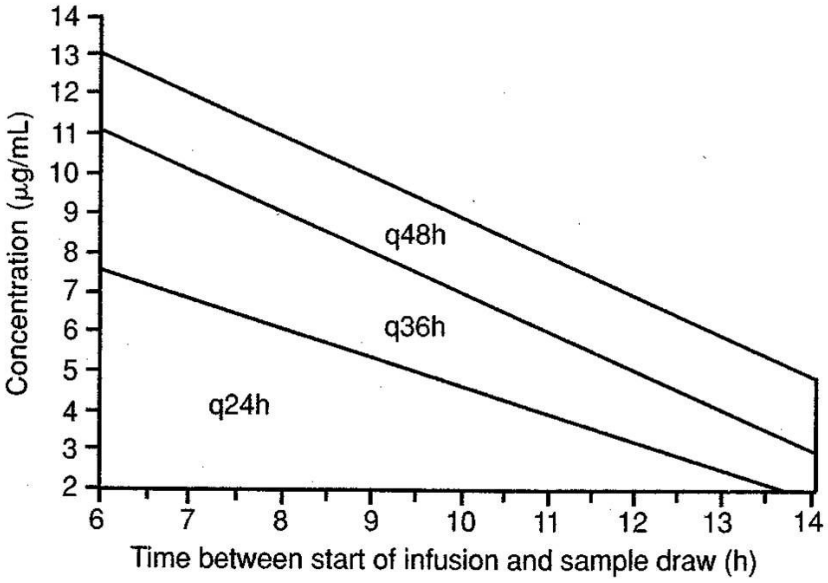
[+]*Pharmacokinetics consult recommended*

3. **Scheduling Administration Times**
   - Scheduled dosing times should be adhered to & communicated to nursing
     - e.g., If patient receives an initial tobramycin dose at 1600 on Monday, they should NOT receive the same large dose at 0800 on Tuesday)

4. **Labs/Monitoring** – The following laboratory orders are also recommended upon entering the order for an aminoglycoside:
   - **SCr/BUN**: every 1-2 days
   - **Random level:** *6-14 hours* after the **1st dose administered**
     - Interpret random level on the nomogram (see below)
     - Recheck random level (6-14h post-dose) *every 5-7 days* if SCr/BUN stable
     - If renal function unstable, recheck until stable, and then check every 5-7d
   - Alternative monitoring method: draw a trough just **before the 2nd dose**
     - Goal trough G/T < 1mcg/mL, Amikacin < 4mcg/mL
   - Monitoring peak concentrations is not necessary
     - Anticipated to be **~ 20mcg/mL** for gentamicin/tobramycin

5. **Random Level Interpretation:**

The dosing interval should be modified according to the following nomogram:
- Nomogram is based on a dose of 7mg/kg in adult patients



(Nicolau DP, et al. *Antimicrob Agents Chemother* 1995;39: 650-5)

- If the point is on the line, choose the longer interval
- If the random level is off the nomogram at the given time, hold therapy and follow serial levels
  - Re-dose when level < 2mcg/mL (gentamicin/tobramycin)
- For amikacin, divide random by 3, then apply to nomogram

Vancomycin Dosing Guidelines (Adults)

(Rybak M., et al. *Am J Health-Syst Pharm*. 2009;66:82-98.)

- **Loading Dose (LD)**: **20mg/kg*** (max = 2g) is preferred in most circumstances, especially life threatening INFXs
  - *If the patient is severely obese and the dose exceeds 2g, initial doses should be staggered over a short time period (PK consult suggested)*
  - *e.g., 200kg patient could receive ≥ 2g within an 8h period, and then continue with recommended regimen*

- **Maintenance Dose (MD)**: **15-20mg/kg/dose*** using **total body weight**
  - If obese, dose based on AdjBW

Please refer to AMG dosing (page 9) for AdjBW & CrCl calculations

Estimated CrCl (ml/min)	Dosage	Interval
≥ 70	≥ 1000 mg	Q8- 12h
50-69	750 mg	Q12h
30-49	1000 mg	Q24h
15-29	750 mg	Q24h
< 15	15 mg/kg *	Random **
Hemodialysis	LD = 1000mg	x 1 dose
	MD = 500-750mg	Post-HD

* Round dose to the nearest 250 mg increment

** Re-dose when random level approximately < 15 mcg/ml

Modified Lake et al., *Pharmacotherapy* 1985;5(6): 340-4.

Serum Concentration:

Peak Levels: *not necessary*

Trough Levels: *- Once-weekly monitoring is recommended in hemodynamically stable pts.*
- Pre-dialysis troughs are rarely necessary

Goal Serum Trough Concentrations:

Indication	Target
SSTIs, Pyelonephritis	*10 - 15 mcg/mL*
Closed Space Infections (PNA, CNS, Endocarditis, Bone/Joint)	*15 - 20 mcg/mL*

Formulary Guidelines/ Clinical Pearls [G]

Please see MMC intranet (Antimicrobial Stewardship Program)
for an updated listing of various decision support pathways.

Cephalosporins

1. **Cefotaxime** - For use in neonates **ONLY**
   - NOT necessary for the TXT of spontaneous bacterial peritonitis (SBP)
   - Ceftriaxone is a suitable alternative for the treatment of SBP

2. **Ceftriaxone**

   Dose = 1g Q24h, EXCEPT in the following situations:
   - *Closed space infections* (e.g., endocarditis, osteomyelitis) → 2g Q24h
   - *Patients weighing ≥ 100kg* → 2g Q24h
   - *Meningitis* (d/t resistant *S. pneumoniae*) → 2g Q12h

3. **Cefoxitin**
   - NOT considered a therapeutic agent due to significant resistance

4. **Cefepime**
   - To maximize pharmacodynamic properties may consider empiric **Q8h** dosing in patients with suspected *P. aeruginosa* INFXs and CrCl > 60mL/min
   - Dose *may* potentially be de-escalated once susceptibilities/MIC are known depending on site of INFX and patients weight

3rd Generation Cephalosporins (e.g., ceftriaxone, ceftazidime, cefdinir)
- Are known potent inducers of chromosomal β-lactamase production (predominately AmpC) in species-specific bugs (aka, SPACE/SPICE):
  - *Serratia, Pseudomonas, Acinetobacter,* indole-*positive proteae (Morganella), Citrobacter,* & *Enterobacter species*
- Although isolates may initially test as "susceptible" to 3rd generation cephalosporins, resistance can emerge during txt with these antibiotics
- Cefepime (4th generation cephalosporin) does NOT induce AmpC production and is stable in the presence of AmpC, thus it is the drug of choice (along with carbapenems) when treating SPACE/SPICE organisms

Penicillins

1. **Ampicillin/Sulbactam**
   - Combined use with metronidazole not warranted*

2. **Piperacillin/Tazobactam**
   - Zosyn 3.375g IV Q6h = 12g of Piperacillin/1.5g Tazobactam
   - TXT of documented or empiric *P. aeruginosa* PNA requires at least 16g of piperacillin/day (e.g., 3.375g IV Q4h or 4.5g IV Q6h)
     - Must be combined with an aminoglycoside during initial presumptive txt of nosocomial PNA; may be discontinued if *P. aeruginosa* is NOT isolated
   - Combined use with metronidazole not warranted*

Miscellaneous

1. **Trimethoprim/Sulfamethoxazole**
   - **IV:** 1 Ampule = 80mg TMP/400mg SMX
     - Dilution: 5mL TMP/SMX in 125mL D_5W
     - *If fluid restricted, 5mL TMP/SMX in 75mL D_5W*
   - **Tablet**: 1 DS Tablet = 160mg TMP/800mg SMX
   - **Suspension:** 20ml = 1 DS Tablet

2. **Aztreonam**
   - A monobactam ABX with activity against *gram-negative* bacteria ONLY
   - Can be safely used in IgE mediated penicillin-allergic patients

3. **Nitrofurantoin** – Immediate Release
   - MMC does not supply the sustained release formulation (Macrobid)
   - Indicated for the TXT of uncomplicated UTIs ONLY, secondary to its poor tissue penetration and low serum concentrations (Dose = 100mg Q6h x 7d)
   - Contraindicated in patients with CrCl < 40ml/min
     - Inadequate urinary concentrations and potential for toxicity

4. **Daptomycin ®**
   - Daptomycin has been associated with CK elevations
     - Baseline and weekly monitoring is recommended
   - Daptomycin bone penetration is poor; concerns exist regarding the rapid development of resistance especially in the of setting osteomyelitis txt
   - Daptomycin should be dose based on actual body weight
     - In obese patients cost can be considerable (i.e., a 120kg pt. receiving 6mg/kg/day = ~ $306/day)

5. **Doripenem**
   - To optimize PK/PD properties, 1g Q8h, infused over 4h has been studied in critically ill patients with HAP/VAP (Ambruzs M. et al. ICAAC 2009)
     - Option for prolonged infusion is built into SCM ordering screens
   - Isolates that are susceptible to meropenem and imipenem are generally susceptible to doripenem; however some isolates that are intermediate or resistant to other carbapenems may be susceptible to doripenem
     - Further susceptibility testing required, call lab (885-7895) to request E-Test

6. **Meropenem**
   - Use restricted to pediatric and cystic fibrosis patients

7. **Metropime (Metronidazole + Cefepime)**
   - The combination of metronidazole and cefepime (in the same minibag) has a similar spectrum of activity as piperacillin/tazobactam
     - Only exception: Metropime lacks activity against *Enterococcus spp.*
   - Substitution of Pip/Tazo with Metropime is strongly encouraged in most circumstances because of the numerous benefits associated with its use:
     - Decreased cost (approximately a 30% cost savings)
     - Decreased nursing administration time
     - Increased heterogenicity of ABX use
   - Available for ordering in SCM under "Metropime"

8. **Clindamycin**
   - Combined use with metronidazole not warranted*
   - Doses (IV) in excess of 600mg do not contribute to increased efficacy, thus a max dose of 600mg IV Q8h is recommended in non-obese pts.

9. **Metronidazole**
   - Combined use with Amp/Sulbactam or Pip/Tazo not warranted*
   - Because of its T½ (~9 hours), metronidazole is preferred to be adm. on an every 12h schedule (IV and PO) in non-obese individuals
   - Drug of choice for initial episode or 1st recurrence of **mild-moderate** *C. difficile* infection (Dose = 500mg PO Q8h x 10-14 days)

10. **Oral Vancomycin**
    - Drug of choice for an initial episode of **severe** CDI, or txt of 2nd or later recurrence (Dose = 125mg PO Q6h x 10-14 days)
    - Oral vancomycin absorption is negligible, thus high fecal concentrations are achieved following administration of conventional doses (125mg Q6h), thus higher doses are unwarranted

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* Combination use may rarely be necessary if concurrently treating *C. difficile*

Anitfungals

1. **Fluconazole**
   - If rifampin is used concurrently, the dose of fluconazole must be doubled due to CYP450 induction of fluconazole metabolism
   - Fluconazole exhibits dose-dependent susceptibility against *C. glabrata*
     - Doses of 12mg/kg (70kg pt. = 800mg) are required

2. **Voriconazole ®**
   - Oral voriconazole is ~ 96% bioavailable, thus PO is preferred when feasible
   - The IV formulation is solubilized in a nephrotoxic carrier, thus is NOT recommended in patients with CrCl < 50mL/min or in those receiving any form of dialysis (e.g., HD, CVVH, peritoneal)
   - Voriconazole is a potent inhibitor of CYP enzymes 2C9, 2C19 > 3A4 thus has the potential for significant drug interactions which should be screened for
     - Concurrent use of the following agents is **contraindicated**:

Significant ↓ in Voriconazole Exposure due to CYP induction	**Significant ↑ in Drug Exposure due to CYP inhibition by Voriconazole**
- Rifampin & Rifabutin - Ritonavir High-dose (400mg Q12) - Carbamazepine - Long Acting barbiturates - St. Johns Wort	- Sirolimus - Terfenadine - Astemizole - Cisapride - Pimozide - Quinidine

3. **Amphotericin B Lipid Complex (Abelcet, ABLC)**

Initial use of lipid-based amphotericin B (*without a challenge of conventional amphotericin B*) is reserved for the following situations:

1. Baseline SCr > 2.5 mg/dl ***or*** calculated/measured CrCl of ≤40 ml/min

AND

2. Not maintained on chronic hemodialysis or peritoneal dialysis
3. Prior history of intolerance - needs to be evaluated on a case by case basis

Use of lipid-based amphotericin B may be initiated during a course of therapy with conventional amphotericin B for the following indications:

1. <u>Amphotericin B Induced Nephrotoxicity</u>
   - An increase of >1.5 mg/dl in SCr compared with baseline immediately prior to conventional amphotericin B therapy

   AND

   - Standard measures including pre- and post-dose hydration with saline have been employed

   AND

   - Unable to avoid concurrent nephrotoxins

   AND

   - A minimum trial of 5 doses or 3.0 mg/kg of conventional amphotericin B has been completed (*e.g., 0.6 mg/kg daily dose x 5 doses = 3.0 mg/kg*)

2. Failure of conventional ampho B* in documented fungal INFXs as evidenced by:
   *After a minimum course of 500 mg or 7.0 mg/kg of amphotericin B
   (*e.g., 1.0 mg/kg daily dose x 7 doses = 7.0 mg/kg total dose*)

   - Clinical progression (increased cough, chest pain, sputum, etc.)

   OR

   - Radiographic progression

   OR

   - Pathological progression

3. Severe unrelenting infusion related reactions
   - Defined as rigors, fevers, and hypotension that are refractory to standard pre-medications (e.g., Acetaminophen, diphenhydramine, meperidine, & hydrocortisone)

The use of lipid-based amphotericin B must be re-evaluated weekly. Conventional amphotericin B should be restarted in those patients whose clinical conditions no longer require lipid-based amphotericin B.

Formulary Restrictions

The following agents are restricted to Infectious Diseases approval only; no consultation is required. In order to dispense these agents in accordance with the Pharmacy & Therapeutics Committee policy, one must seek approval from one of the following contacts: Antimicrobial Stewardship Program team member, adult or pediatric ID attending physicians, or current ID fellows.

Valganciclovir

Criteria for Use:

- Treatment of documented CMV disease as an alternative to IV ganciclovir
- Prophylaxis in CMV positive donor recipients

Voriconazole

Criteria for Use:

- Proven or probable invasive aspergillosis (primary or salvage)
- *Scedosporium* and *Fusarium* spp. INFXs (1st Line)
- Invasive Candida infections resistant to fluconazole
  - e.g., *C. glabrata* & *C. krusei* AND refractory to amphoB
- NOT INDICATED for empirical txt of fever & neutropenia

Dosing	Intravenous	Oral	
		< 40kg	**≥ 40kg**
Loading	6mg/kg Q12h x 2 doses	200mg Q12h x 2 doses	400mg Q12h x 2 doses
Maintenance	4mg/kg Q12h	100mg Q12h	200mg Q12h

Daptomycin

Criteria for Use:

- Txt of multi-drug resistant Gram-positive (VRE, MRSA) serious INFX where no other alternatives exist (NOT effective for pneumonia)
- Severe intolerance to vancomycin after pre-meds have failed AND the pathogen is not susceptible to other alternatives

FDA Approved Indications:

- Bacteremia, including those with Right-sided endocarditis, caused by MSSA and MRSA (Dose = 6mg/kg)
- Complicated skin/soft tissue infections (Dose = 4mg/kg) due to:
  - *S. aureus* (including MRSA)
  - *Streptococcus pyogenes, agalactiae, dysgalactiae subspecies, equisimilis*
  - *Enterococcus faecalis* (vancomycin susceptible only)*

** Daptomycin has activity against VRE although not FDA approved*

Linezolid

Criteria for Use:

- VRE infections in which the ampicillin MIC is >64 mcg/ml
- Urinary tract infections caused by VRE when CrCl < 40 ml/min
  - Otherwise nitrofurantoin is recommended
- Unsuccessful or delayed initial attempts at insertion of a central or peripheral catheter (PO linezolid >90% bioavailable)
- Empiric therapy for patients with ventilator-/hospital-acquired PNA if GPC seen on gram stain from respiratory source **AND**
  - The patient has impaired renal function (CrCl < 20mL/min) AND is concurrently receiving an aminoglycoside **-OR-**
  - The patient has developed PNA while receiving vancomycin
- Severe intolerance to vancomycin after pre-meds have failed and the pathogen is not susceptible to other alternatives
  - Se*vere intolerance defined as:* severe rash (immune-complex mediated), determined to be directly related to vancomycin
  - *Red-Man's Syndrome* (Histamine-mediated) *refractory* to traditional countermeasures (e.g., prolonged infusion, diphenhydramine)

Micafungin

Criteria for Use:

- Invasive candida infections resistant to fluconazole
  - e.g., *C. glabrata/C. krusei* AND refractory to ampho B
- Prophylaxis of candida infections in hematopoietic stem cell transplant patients intolerant to conventional therapy
- Treatment of azole resistant esophageal candidiasis

MMC Antibiogram

Antibiotic Susceptibility, January through December 2009

Duplicate isolate eliminated* % Susceptible

	K.pneumoniae	*M. morganii*	*P. mirabilis*	*P. Aeruginosa*	*S. marcescens*	*A. baum/haem*
Amikacin	99%	100%	100%	87%	98%	96%
Amox/Clav	97%	8%	99%	—-	4%	—-
Ampic/Sulb	87%	4%	92%	—-	9%	79%
Ampicillin	7%	0%	89%	—-	5%	—-
Aztreonam	98%	80%	99%	74%	93%	—-
Cefazolin	96%	0%	93%	—-	0%	—-
Cefepime	99%	100%	99%	83%	100%	96%
Cefotaxime	98%	88%	99%	17%	88%	79%
Cefoxitin	91%	88%	100%	—-	30%	—-
Ceftazidime	98%	88%	99%	92%	88%	96%
Ceftriaxone	98%	96%	99%	34%	96%	75%
Cefuroxime	91%	8%	99%	—-	0%	—-
Cephalothin	85%	0%	95%	—-	0%	—-
Ciprofloxacin	94%	84%	77%	68%	89%	86%
Ertapenem	99%	100%	100%	—-	98%	—-
Gentamicin	98%	88%	92%	78%	98%	96%
Imipenem	100%	92%	99%	87%	98%	96%
Levofloxacin	96%	88%	90%	70%	98%	89%
Meropenem	99%	100%	100%	87%	98%	95%
Piperac/Tazo	98%	96%	100%	86%	80%	—-
Piperacillin	71%	56%	90%	93%	86%	86%
Tetracycline	87%	48%	3%	—-	23%	100%
Tobramycin	98%	92%	93%	88%	86%	96%
Trim/Sulfa	94%	72%	89%	—-	100%	89%

	% Susceptible	% Intermediate
H. influenzae	*S. pneumoniae*	*S. pneumoniae*
Ampicillin	74%		
Cefaclor	78%		
Cefotaxime	100%		
Ceftriaxone	100%	99%	1%
Ceftriaxone (Menin)	—-	96%	3%
Clindamycin	—-	86%	—-
Erythromycin	—-	67%	2%
Meropenem	—-	93%	3%
Moxifloxacin	—-	100%	—-
Penicillin	—-	78%	16%
Tetracycline	—-	86%	—-
Trim/Sulfa	78%	—-	—-
Vancomycin	—-	100%	—-

*Duplicate isolate: Same patient, same organism, same body site, within 3 days'

MMC Antibiogram (Cont'd) % Susceptible

	C. freundii	*C. koseri*	*E. aerogenes*	*E. cloacae*	*E. coli*	*K. oxytoca*
Amikacin	100%	100%	100%	100%	100%	99%
Amox/Clav	12%	94%	0%	1%	86%	85%
Ampic/Sulb	65%	100%	37%	25%	66%	55%
Ampicillin	33%	6%	3%	7%	63%	5%
Aztreonam	83%	100%	89%	85%	98%	88%
Cefazolin	8%	94%	0%	0%	91%	44%
Cefepime	100%	100%	100%	95%	98%	93%
Cefotaxime	83%	100%	94%	82%	98%	93%
Cefoxitin	8%	100%	6%	2%	96%	96%
Ceftazidime	83%	100%	91%	86%	97%	93%
Ceftriaxone	83%	100%	91%	84%	97%	89%
Cefuroxime	69%	89%	69%	38%	95%	77%
Cephalothin	2%	94%	0%	0%	61%	49%
Ciprofloxacin	90%	100%	100%	97%	84%	93%
Ertapenem	100%	100%	100%	99%	100%	99%
Gentamicin	94%	100%	94%	95%	94%	92%
Imipenem	100%	100%	100%	99%	100%	100%
Levofloxacin	92%	100%	100%	98%	84%	95%
Meropenem	100%	100%	100%	98%	100%	100%
Piperac/Tazo	94%	100%	89%	93%	98%	86%
Piperacillin	77%	67%	86%	77%	65%	54%
Tetracycline	85%	100%	91%	93%	80%	88%
Tobramycin	96%	100%	91%	96%	94%	90%
Trim/Sulfa	87%	100%	97%	91%	79%	96%

	E. faecalis	E. faecium	S. aureus	S.epidermidis	MSSA	MRSA
Amox/Clav	—-	—-	64%	37%	100%	—-
Ampic/Sulb	—-	—-	64%	37%	100%	—-
Ampicillin	100%	21%	0%	0%	0%	—-
Cefazolin	—-	—-	64%	37%	100%	—-
Ceftriaxone	—-	—-	64%	37%	100%	—-
Clindamycin	—-	—-	91%	70%	97%	82%
Erythromycin	33%	14%	49%	38%	71%	8%
Gentamicin	—-	—-	99%	80%	99%	99%
Imipenem	—-	—-	64%	37%	100%	—-
Levofloxacin	77%	13%	71%	47%	94%	29%
Meropenem	—-	—-	65%	35%	100%	0%
Moxifloxacin	—-	—-	81%	67%	97%	51%
Oxacillin	—-	—-	64%	37%	100%	—-
Penicillin	100%	21%	13%	9%	20%	—-
Rifampin	69%	21%	99%	97%	99%	99%
Tetracycline	26%	67%	95%	89%	94%	96%
Trim/Sulfa	—-	—-	99%	60%	100%	99%
Vancomycin	100%	27%	100%	100%	100%	100%

Dosage of Antimicrobial Agents in Obesity

- There has been a dramatic increase in adult obesity (BMI $\geq$ 30 kg/m^2) in the United States throughout the past two decades [1]
- The CDC estimates a quarter of Maine's residents are obese[1]
- Due to physiological and pharmacokinetic (PK) alterations associated with obesity (↑Vd & clearance)[2], use of conventional doses (based on 70kg pt.) may not be adequate to achieve minimal effective concentrations
- Tailoring the dosing of antimicrobial agents based on individual characteristics (e.g., wgt, CrCl, INFX) is recommended to achieve maximum efficacy & safety
- With the exception of the AMGs and vancomycin, PK data regarding optimal dosing of antimicrobial agents in obese individuals is lacking
- The following charts are meant to serve as a guide in dosing obese & morbidly obese individuals based on limited available literature

Weight Based ABX Dosing

Drug	Non-Obese	Obesity*
Antibacterials		
Aminoglycosides	IBW	AdjBW
Daptomycin	TBW	TBW
Vancomycin	TBW	AdjBW
Antifungals		
Amphotericin B	TBW	TBW
Amphotericin Lipid	TBW	AdjBW
Antivirals		
Acyclovir	IBW	IBW

TBW = Total Body Weight, IBW = Ideal body weight
AdjBW = Adjusted Body Weight (See pg. 9 for calculations)

Suggested Regimens in Obese (30-39.9 kg/m^2) and Morbidly Obese ($\geq$40 kg/m^2) Patients☆

Antibiotic	Suggested Regimen*
Aztreonam	2g Q6-8hr
Cefazolin	2g Q6-8hr
Cefepime	2g Q8hr
Ceftriaxone	2g Q12-24hr
Doripenem	1g Q8hr
Ciprofloxacin	400mg *IV* Q8h or 750mg *PO* Q12h
Mino/Doxy-cycline	100mg Q AM + 200mg QHS
Linezolid	500mg Q8hr

☆ Assuming normal hepatic function & CrCl > 50mL/min

* Pts. weighing in excess of 150kg may warrant further discussion with a clinical specialist

1. Flegal KM, Carroll MD, Ogden CL, et al. JAMA 2010;303(3):235-41.
2. Bearden DT, Rodvold KA. Dose adjustments for antibacterials in obese patients: applying clinical pharmacokinetics. Clin Pharmacokinetics 2000;38:415-26.
3. Stein GE, et al. Ann Pharmacotherapy 2005;39:427-32.
4. Pawsey SD, et al. (1996). U-1007666 safety, toleration and pharmacokinetics after oral and intravenous administration. In Abstracts of the First European Congress of Chemotherapy, Glasgow, UK. Abstract
F151. Federation for the Societies for European Chemotherapy and Infection, London, UK.

Adult Dosage of Antimicrobial Agents in Renal Impairment

Agents Requiring NO Dosage Adjustments with Concurrent Renal Insufficiency		
Azithromycin	Linezolid	Amphotericin B
Ceftriaxone*	Metronidazole	Ampgotericin B Lipid (Abelcet)
Clindamycin	Minocycline	Micafungin
Dicloxacillin	Moxifloxacin	Voriconazole♦
Doxycycline	Oxacillin	Rifampin
		Isoniazid
* *Unless concurrent hepatic impairment*		♦*Oral Only*

Adjustment for Renal Impairment based on CrCl					
DRUG	> 50 mL/min	10- 50mL/min	< 10mL/min	Hemodialysis*	CVVH**
Aminoglycosides					
Amikacin (IV)	see dosage guidelines (pg. 11-14)			3mg/kg Post-HD	7.5mg/kg Q24-48h
Gentamicin (IV)	see dosage guidelines (pg. 11-14)			1mg/kg Post-HD	1.5-2.5mg/kg Q24-48h
Tobramycin (IV)	see dosage guidelines (pg. 11-14)			1mg/kg Post-HD	1.5-2.5mg/kg Q24-48h
Penicillins					
Amoxicillin (PO)	500mg Q8h	500mg Q12h	500mg Q24h	500mg Q24h	N/A
Ampicillin (IV)	1-2g Q6h	1-2g Q6-12h	1-2g Q12-24h	1-2g Q8-12h	1-2g Q8-12h
Ampicillin/Sulbactam (IV)	1.5-3g Q6h	1.5g-3g Q8-12h	1.5g-3g Q12-24h	1.5g Q12h	1.5-3g Q8-12h
Penicillin G (IV)	0.5-4 millionU Q4h	↓ dose by 25%	↓ by 50-80%	1-2 millionU Q6h	4 millionU Q8h
Pipericillin/Tazo (IV) *P. aeruginosa*	3.375g-4.5g Q6h 4.5g Q6h	2.25g Q6h 4.5g Q8h	2.25g Q8h 4.5g Q12h	2.25g Q8h 2.25g Q6h	2.25g Q6h - 3.375g Q8h

%: Represents % dosage decrease in the presence of renal impairment

*Drugs removed by hemodialysis (HD) & continuous ambulatory peritoneal dialysis (CAPD) should be dosed for CrCl < 10ml/min unless specified otherwise. Drugs cleared by HD should be scheduled for administered after HD.

**Drugs removed by continuous veno-venous filtration (CVVH) should be dosed for CrCl 10-15ml/min unless specified otherwise.

***Drugs removed by continuous veno-venous hemodialysis (CVVHD) should be dosed for CrCl 10-50ml/min unless specified otherwise.

Adjustment for Renal Impairment based on CrCl					
DRUG	> 50 mL/min	10- 50mL/min	< 10mL/min	Hemodialysis*	CVVH**
Cephalosporins					
Cefazolin (IV)	1-2g Q8h	1-2g Q12h	1-2g Q24-48h	1g Q24h	1-2g Q12h
Cephalexin (PO)	250-500mg Q6h	250-500mg Q12h	250-500mg Q12h	500mg Q24h	N/A
Cefdinir (PO)	300mg Q12h	300mg Q24h	300mg Q24h	300mg Q48h	N/A
Ceftazidime (IV)	1-2g Q8h	1-2g Q12-24h	0.5-1g Q 24-48h	1g Post-HD	1-2g Q12h
Cefepime (IV) *Meningitis* *P. aeruginosa*	1-2g Q8-12h 2g Q8h 2g Q8h	1-2g Q24h 2g Q12h 1g Q12h	1g Q24h 2g Q24h 1g Q24h	1g Q24h 2g Q24h 1g Q24h	 1-2g Q12h
Carbapenems					
Meropenem (IV)	1-2g Q8h	1g Q8-12h	0.5g-1g Q24h	0.5-1g Q24h	0.5-1g Q12h
Doripenem (IV)	0.5g-1g Q8h	250mg Q8-12h	250mg Q 12-24h	250mg Q12h or 500mg Q24h	250-500mg Q8h

Adjustment for Renal Impairment based on CrCl					
DRUG	> 50 mL/min	10- 50mL/min	< 10mL/min	Hemodialysis*	CVVH**
Miscellaneous					
Aztreonam (IV)	1-2g Q8h	0.5-1.0 g Q8h	250-500mg Q8h	500mg Post-HD	1-2g Q12h
Ciprofloxacin (IV) (PO)	400mg Q8-12h 500-750mg Q12h	400mg Q12-24h 250-500mg Q12h	400mg Q24h 500-750mg Q24h	200-400mg Q24 250-500mg Q24	200-400mg Q12- N/A
Daptomycin (IV)	4-6mg/kg Q24h	4-6mg/kg Q24-48h	4-6mg/kg Q48h	4-6mg/kg Q48h	4-6mg/kg Q48
TMP/SMX (IV) (PO)	5mg/kg (TMP) Q6-12h 160/800mg Q8-12h	2.5-5mg/kg Q12h ↓dose 50% Q24h	2.5-5mg/kg Q12-24h Avoid	5mg/kg Post-HD PCP: 80/400mg Q24h	2.5-7.5mg/kg (TM Q12h N/A
Vancomycin (IV)	See dosage guidelines (pg.13) 500-750mg			500-750mg Post-HD	10-15mg/kg Q2 48h
Nitrofurantoin (PO)	50-100mg Q6h	Avoid < 40mL/min (therapeutic levels not attained in urine)			N/A
Antituberculosis Agents					
Ethambutol (PO)	15-25mg/kg Q24h	15-25mg/kg Q24-36h	15-25mg/kg Q48h	15-25mg/kg Post-HD	N/A
Ethionamide (PO) (Max =1g/day)	250-500mg Q12h	250-500mg Q12h	125-250mg Q12h	125-250mg Q12h	N/A
Pyrazinamide (PO) (Max = 2.5g/day)	25mg/kg Q24 h	25mg/kg Q24h	12-20mg/kg Q24h	12-20mg/kg Post-HD	N/A

Adjustment for Renal Impairment based on CrCl					
DRUG	> 50 mL/min	10- 50mL/min	< 10mL/min	Hemodialysis*	CVVH**
Antivirals					
Acyclovir (IV) (PO)	5-10mg/kg Q8h 200-800mg 5x/day	5-10mg/kg Q12-24h 200-800mg Q8h	2.5-5mg/kg Q24h 200-800mg Q12h	2.5-5mg/kg Q24h Post-HD	5-10mg/kg Q24h N/A
Foscarnet (IV)	Refer to 2010 Sanford Guide for Maintenance & Induction Dosing Regimens				N/A
Ganciclovir (PO)	0.5-1g Q8h	0.5-1g Q24h	0.5g 3x/week	0.5g 3x/week Post-HD	N/A
Ganciclovir (IV) *INDUCTION*: *MAINTENCE*:	2.5-5mg/kg Q12h 2.5-5mg/kg Q24h	1.5-2.5mg/kg Q24h 0.625-1.25mg/kg Q24h	1.25mg/kg 3x/wk 0.625mg/kg 3x/wk	1.25mg/kg 3x/wk Post-HD 0.6mg/kg 3x/wk Post-HD	2.5mg/kg Q24h 1.5mg/kg Q24h
Valganciclovir (PO) Induction: Maintenance:	900mg Q12h 900mg Q24h	450mg Q12-24h 450mg Q24-48h	450mg Q48h 450mg 2x/wk	900mg Q48h 450mg Q48h	N/A
Valacyclovir (PO)	1g Q8-12h	1g Q12-24h	500mg Q24h	500mg Q24h	500mg Q24h
Oseltamivir (PO) *Treatment:* *Prophylaxis:*	75mg Q12h 75mg Q24h	75mg Q24h 75mg Q48h	75mg Q24h 75mg Q48h	30mg Post-HD every other session	75mg Q12-24h

Adjustment for Renal Impairment based on CrCl					
DRUG	> 50 mL/min	10- 50mL/min	< 10mL/min	Hemodialysis*	CVVH**
Antifungals					
Fluconazole (IV/PO)	400-800mg Q24h	↓ 50% Q24h	↓ 50-75% Q24h	200-400mg Post-HD	200-400mg Q24h
Voriconazole (IV)	6mg/kg x2 doses, then 4mg/kg Q12h	Avoid – 2° to Accumulation of neprotoxic carrier			200mg *PO* Q12h
Flucytosine (PO)	25mg/kg Q6h	25mg/kg Q12-24h	25mg/kg Q24-48h	25mg/kg Q24-48h Post-HD	25mg/kg Q12-24h

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