

# Guidelines for Antimicrobial Usage

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2011-2012



**Cleveland Clinic**

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Cleveland Clinic

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# Introduction

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The majority of hospitalized patients receive antimicrobials for therapy or prophylaxis during their inpatient stay. It has been estimated that at least fifty percent of patients receive antimicrobials needlessly. Reasons include inappropriate prescribing for antimicrobial prophylaxis, continuation of empiric therapy despite negative cultures in a stable patient, and a lack of awareness of susceptibility patterns of common pathogens. Over prescribing not only increases the costs of health care, but may result in superinfection due to antimicrobial-resistant bacteria, as well as opportunistic fungi, and may increase the likelihood of an adverse drug reaction. On the other hand, not prescribing (when there is an urgent need at the bedside) may also lead to serious consequences.

The materials in this booklet constitute guidelines only and are subject to change pursuant to medical judgement relative to individual patient needs. Our antimicrobial formulary decisions are made annually after thorough deliberations and consensus building with members of the Infectious Disease Department, the Department of Pharmacy, and the Section of Microbiology. *In vitro* susceptibility data of the previous year are shared and emerging resistance patterns reviewed. Usage and cost data are discussed. The mission of our program is to provide the most cost-effective antimicrobial agents to our patients.

This booklet does not contain specific guidelines for treatment of human immunodeficiency virus (HIV) infection. Nor is prophylaxis against opportunistic microorganisms included, since such issues are usually handled in our outpatient clinics. Similarly, treatment of infectious diseases commonly seen in the outpatient setting, such as otitis media and pharyngitis, are not included in this booklet.

# TABLE 1 Guidelines<sup>1</sup> for Interpretation of Gram Stain Results

## Gram-Positive Cocci (GPC)

- Pairs, chains, clusters:
  - *Staphylococcus* sp
- Pairs, chains:
  - *Streptococcus* sp
  - *Enterococcus* sp
- Pairs, lancet-shaped:
  - *Streptococcus pneumoniae*
- Pairs:
  - *Enterococcus* sp

## Gram-Positive Bacilli (GPB)

- Diphtheroids:
  - Small, pleomorphic:
    - › *Corynebacterium* sp
    - › *Propionibacterium* (anaerobe)
- Large, with spores:
  - *Clostridium* sp
  - *Bacillus* sp
- Branching, beaded, rods:
  - *Nocardia* sp
  - *Actinomyces* sp (anaerobe)
- Other:
  - *Listeria* sp (blood/cerebrospinal fluid)
  - *Lactobacillus* sp (vaginal/blood)

## Gram-Negative Cocci (GNC)

- Diplococci
  - Pairs:
    - › *Neisseria meningitidis*
    - › *Neisseria gonorrhoeae*
    - › *Moraxella catarrhalis*
- Other:
  - *Acinetobacter* sp

## Gram-Negative Bacilli (GNB)

- Enterobacteriaceae:
  - *Escherichia coli*
  - *Serratia* sp
  - *Klebsiella* sp
  - *Enterobacter* sp
  - *Citrobacter* sp
- Nonfermentative:
  - *Pseudomonas aeruginosa*
  - *Stenotrophomonas (Xanthomonas) maltophilia*
  - Many others
- *Haemophilus influenzae*
- *Bacteroides fragilis* group (anaerobe)
- Fusiform (long, pointed):
  - *Fusobacterium* sp (anaerobe)
  - *Capnocytophaga* sp

<sup>1</sup> These guidelines are not definitive but presumptive for the identification of organisms on gram stain. Treatment will depend on the quality of the specimen and appropriate clinical evaluation.

## TABLE 2 Key Characteristics of Selected Organisms

### Gram-Positive Cocci (GPC)

- Catalase-positive:
  - *Staphylococcus* sp
- Catalase-negative:
  - *Enterococcus* sp
  - *Streptococcus* sp (chains)
  - *Micrococcus* sp (usually insignificant)
- Coagulase-positive:
  - *Staphylococcus aureus*
- Coagulase-negative:
  - Coagulase-negative staphylococci (CNS):
    - › Blood: *Staphylococcus epidermidis* or CNS
    - › Urine: *Staphylococcus saprophyticus*
    - › *Staphylococcus lugdunensis*<sup>4</sup>

### Gram-Positive Bacilli (GPB)

- Diphtheroids:
  - May be *Corynebacterium* sp: often blood culture contaminants
  - *Corynebacterium jeikeium*: resistant to many agents except vancomycin
- Anaerobic diphtheroids: *Propionibacterium acnes*
- *Bacillus* sp: *Bacillus anthracis*: non-motile and non- $\beta$ -hemolytic; *Bacillus cereus*; *Bacillus subtilis*, ie, large, “box car” rods with spores
- *Listeria monocytogenes*: cerebrospinal fluid, blood
- *Lactobacillus* sp: vaginal flora, rarely in blood
- *Nocardia* sp: Branching, beaded; partial acid-fast-positive
- Rapidly growing mycobacteria:
  - *Mycobacterium fortuitum*
  - *Mycobacterium chelonae/abscessus*

### Gram-Negative Cocci (GNC)

- *Neisseria meningitidis*
- *Neisseria gonorrhoeae*
- *Moraxella (Branhamella) catarrhalis*
- *Acinetobacter* sp<sup>1</sup>

### Gram-Negative Bacilli (GNB)

- Lactose-positive:
  - *Escherichia coli*
  - *Klebsiella pneumoniae* (mucoid)
  - *Enterobacter* sp<sup>2</sup>
  - *Citrobacter* sp<sup>2</sup>
- Lactose-negative/oxidase-negative:
  - *Proteus mirabilis*: indole-negative
  - *Proteus vulgaris*: indole-positive
  - *Providencia* sp
  - *Morganella morganii*
  - *Serratia* sp<sup>3</sup>
  - *Salmonella* sp
  - *Shigella* sp
  - *Acinetobacter* sp<sup>1</sup>
  - *Stenotrophomonas (Xanthomonas) maltophilia* (nonfermenter)
- Lactose-negative/oxidase-positive:
  - *Pseudomonas aeruginosa* (green; “grape odor”)
  - *Aeromonas hydrophila* (may be lactose-positive)
  - Rare:
    - › Other *Pseudomonas* sp
    - › *Moraxella* sp<sup>1</sup>
    - › *Alcaligenes* sp
    - › *Burkholderia* sp

(Table continued on following page)

**TABLE 2 Key Characteristics of Selected Organisms** *(continued)*

**Gram-Negative Bacilli (GNB)**

- Other:
  - *Haemophilus influenzae* (coccobacillary); requires supplements/special media (chocolate agar plate)

**Fungi**

- Molds:
  - Aseptate hyphae:
    - › Zygomycetes, such as:
      - *Rhizopus* sp
      - *Mucor*
  - Septate hyphae:
    - › Brown pigment (phaeohyphomycetes), such as:
      - *Bipolaris* sp
      - *Exserohilum* sp
      - *Alternaria* sp
      - *Curvularia* sp
      - *Sporothrix schenckii* (“rose-gardeners”)
    - › Non-brown pigmented (hyalohyphomycetes, most common), such as:
      - *Aspergillus* sp (*Aspergillus fumigatus*, *Aspergillus flavus*)
      - *Fusarium* sp
      - *Penicillium* sp
      - *Paecilomyces* sp
      - Dermatophytes

- Thermally dimorphic (yeast in tissue, mold in lab):
  - › *Histoplasma capsulatum* (slow growing)
  - › *Blastomyces dermatitidis*
  - › *Coccidioides immitis*
- Yeast:
  - *Candida* sp; *Candida albicans* if germ tube-positive
  - *Cryptococcus* sp (no pseudohyphae); *Cryptococcus neoformans* if latex- or CAD-positive
  - *Candida glabrata*
  - *Trichosporon* sp
  - *Rhodotorula*, *Saccharomyces* sp

**Anaerobes**

- GNB:
  - *Bacteroides* sp (*Bacteroides fragilis*)
  - *Fusobacterium* sp
- GNC:
  - *Veillonella* sp
- GPC:
  - *Peptostreptococcus* sp
- GPB:
  - *Propionibacterium acnes*
  - *Clostridium* sp (spores)
  - *Actinomyces* sp (branching, filamentous)
  - *Lactobacillus* sp
  - *Eubacterium* sp
  - *Bifidobacterium* sp

1 May be either bacillary or coccoid.

2 May be lactose negative.

3 May produce red pigment and appear lactose-positive initially.

4 Clinically can act as *Staphylococcus aureus*; laboratory results will reflect this by using MIC interpretation for *Staphylococcus aureus*.



**TABLE 3 Usual Acid-Fast Bacillus Characteristics**

<b><i>Mycobacterium</i> sp</b>	<b>Time to Isolation</b>	<b>Pigment</b>	<b>Usual Clinical Diseases<sup>1</sup></b>
<i>Mycobacterium tuberculosis</i>	10-12 d	None	Pulmonary, extra-pulmonary
<i>Mycobacterium avium complex</i>	5-7 d	None	Pulmonary, extra-pulmonary
<b><i>Mycobacterium gordonae</i></b>	<b>&gt; 10 d</b>	<b>Yellow</b>	<b>Non-pathogenic</b>
<i>Mycobacterium kansasii</i>	10-12 d	Yellow (in light)	Pulmonary, skin and soft tissue
<i>Mycobacterium marinum</i>	10-12 d	Yellow	Skin and soft tissue
<b>Rapid Growers:</b>			
<i>Mycobacterium abscessus</i>	<7 d	None	Skin and soft tissue
<i>Mycobacterium chelonae</i>	<7 d	None	Skin and soft tissue
<i>Mycobacterium fortuitum</i>	<7 d	None	Skin and soft tissue
<b>Partial Acid-Fast Organisms:</b>			
<i>Nocardia</i> sp		Branching, beaded bacilli	Pulmonary, central nervous system, skin and soft tissue
<i>Rhodococcus</i> and <i>Tsukamurella</i> sp		Coccoid, branching, and/or bacillary	Skin and soft tissue, pulmonary

<sup>1</sup> Note: Any acid-fast bacillus may disseminate in immunocomprised hosts.

## TABLE 4 Laboratory Requests and Specimen Types

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1. Blood cultures:
  - a. Blood cultures are most likely to be positive when an ample volume of blood is collected prior to administration of antimicrobials.
  - b. Two sets of 20 mL each should be drawn 1 hour apart, preferably from a peripheral site rather than through a central vascular catheter.
  - c. Ten mL from each blood draw is inoculated into an aerobic bottle and 10 mL into an anaerobic bottle. Cultures are held 4 days before being reported as negative.
  - d. A single positive blood culture of these organisms suggests contamination: *Bacillus* sp, coagulase-negative staphylococci, diphtheroids, *Propionibacterium acnes*, viridans streptococci.
  - e. An isolator tube of 10 mL of blood should be drawn if any of the following are suspected: *Bartonella*, *Bordetella*, *Francisella*, *Histoplasma capsulatum*, *Legionella*, *Mycobacterium* sp. These will be incubated for longer than 4 days before being considered negative.
2. Stools for *Clostridium difficile*:
  - a. Stools are processed for the presence of *Clostridium difficile* toxin by PCR.
  - b. The sensitivity of the assay is >90%.
  - c. **Due to the sensitivity of the assay, only one sample per episode is necessary.**
  - d. Negative results do not rule out the presence of *Clostridium difficile* toxin.
3. Stools for enteric pathogens and ova and parasites:
  - a. Stools sent for bacterial pathogens and parasites should be from outpatients or patients who have been in the hospital <3 days.
  - b. Stools are examined for the presence of *Salmonella* sp, *Shigella* sp, and *Campylobacter jejuni* routinely if submitted for enterics; if for parasites, routine testing for *Giardia* sp and *Cryptosporidium* sp is performed via EIA unless a microscopic examination is specifically ordered.
  - c. Other pathogens require a special request.
4. Antimicrobial susceptibility testing:
  - a. Testing is performed routinely on clinically relevant aerobic bacteria for which there are guidelines as set forth by the Clinical Laboratory Standards Institute (CLSI).
  - b. Requests for susceptibility testing of fungi, non-tuberculosis *Mycobacterium*, and anaerobic bacteria are required.

## TABLE 5 Mechanism of Action of Common Antibacterial Agents

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**Aminoglycosides** interfere with bacterial protein synthesis by binding to 30S and 50S ribosomal subunits.

- Gentamicin
- Tobramycin
- Amikacin

**Beta Lactams:** Penicillins and cephalosporins inhibit bacterial cell-wall synthesis by binding to one or more penicillin-binding proteins which in turn inhibits the final transpeptidation step of peptidoglycan synthesis in bacterial cell walls, thus inhibiting cell-wall biosynthesis. Bacteria eventually lyse due to ongoing activity of organism autolytic enzymes (autolysins and murein hydrolases) while cell-wall assembly is arrested.

### Penicillins

- Amoxicillin
- Ampicillin
- Dicloxacillin
- Oxacillin
- Piperacillin
- Piperacillin/tazobactam

### Cephalosporins

- Cefazolin
- Cefprozil
- Ceftazidime
- Ceftriaxone
- Cefuroxime
- Cephalexin

### Others

- Meropenem
- Aztreonam

**Ciprofloxacin** inhibits DNA-gyrase which does not allow the uncoiling of supercoiled DNA and promotes breakdown of double-strand DNA.

**Clindamycin** binds to the 50S ribosomal subunit (reversibly), preventing peptid-bond formation and inhibiting protein synthesis.

*(Table continued on following page)*

## TABLE 5 Mechanism of Action of Common Antibacterial Agents *(continued)*

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**Daptomycin** acts at the cytoplasmic membrane and is hypothesized to rapidly depolarize the cell membrane via an efflux of potassium and possibly other ions. Cell death occurs as a result of multiple failures in biosystems, including DNA, RNA, and protein synthesis.

**Linezolid** binds to a site on the 23S ribosomal RNA of the 50S subunit, blocking formation of the 70S initiation complex thus inhibiting translation.

**Macrolides** inhibit protein synthesis at the chain elongation step and binds to the 50S ribosomal subunit.

- Erythromycin
- Azithromycin
- Clarithromycin

**Metronidazole** interacts with DNA causing a loss of helical DNA structure and strand breakage, resulting in inhibition of protein synthesis.

**Tetracyclines** inhibit protein synthesis by binding to the 30S and possibly the 50S ribosomal subunits.

- Doxycycline
- Tetracycline

**Tigecycline** binds at the same site on the ribosome as tetracyclines, however binds 5-fold more tightly. Also able to overcome the ribosomal protection mechanism of tetracycline resistance.

**Trimethoprim/sulfamethoxazole:** Trimethoprim inhibits dihydrofolic acid reduction to tetrahydrofolate, resulting in sequential inhibition of the folic acid pathway. Sulfamethoxazole interferes with bacterial folic acid synthesis and growth via inhibition of dihydrofolic acid formation from PABA.

**Vancomycin** inhibits bacterial cell wall synthesis by blocking glycopeptide polymerization through binding to the D-alanyl-D-alanine portion of the cell wall precursor.

**TABLE 6 Guidelines for Treatment of Pneumonia in Adults**

Source/ Setting	Empiric Therapy	Empiric Therapy— Severe Penicillin Allergy <sup>1</sup>	Likely Pathogens	Directed Therapy	Usual Duration
Community <sup>2</sup>	Ceftriaxone + azithromycin	Levofloxacin	<i>Pneumococcus</i> <i>Legionella</i> <i>Mycoplasma</i> <i>Haemophilus influenzae</i> <i>Chlamydia pneumoniae</i> <i>Moraxella catarrhalis</i>	Penicillin G Azithromycin Doxycycline Cefuroxime Doxycycline Cefuroxime	7-14 d
Community- aspiration	Amp/Sulb	Clindamycin	Mouth flora	Amp/Sulb or clindamycin	14 d
Hospital or hospital- aspiration or VAP	Pip/Tazo ± vancomycin ± gentamicin <sup>3</sup>	Ciprofloxacin + vancomycin	<i>Pseudomonas</i> <i>aeruginosa</i> <i>Enterobacter</i> sp  <i>Serratia marcescens</i> <i>Klebsiella</i> sp <i>Acinetobacter</i> sp <i>Staphylococcus aureus</i>	Pip/Tazo + gentamicin <sup>4</sup> Pip/Tazo <sup>6</sup> ± gentamicin Pip/Tazo Pip/Tazo Meropenem <sup>7</sup> Oxacillin <sup>8</sup>	8 d <sup>5</sup>

- 1 For severe penicillin allergy (ie, anaphylaxis). For delayed hypersensitivity reactions (eg, rash to a penicillin), a third-generation cephalosporin (ie, ceftriaxone for CAP/ceftazidime for HAP) or carbapenem may be considered.
- 2 In immunocompromised hosts, consider adding TMP/SMX for *Pneumocystis jirovecii* (*carinii*) coverage.
- 3 Amikacin should be considered in intensive care units where gentamicin/tobramycin susceptibilities are lower.
- 4 Substitute tobramycin if resistant to gentamicin.
- 5 Consider a longer 14-day duration for *Pseudomonas* and *Acinetobacter* HAP.
- 6 For piperacillin/tazobactam-resistant isolates, TMP/SMX or meropenem may be appropriate alternative agents.
- 7 Carbapenem-resistant *Acinetobacter* have been detected. Consider ampicillin/sulbactam or ID consult for alternative therapies.
- 8 Note that 50% of *S aureus* are resistant to oxacillin (or methicillin) and cefazolin. Vancomycin is appropriate in such patients.

**TABLE 7 Guidelines for Treatment of Infective Endocarditis in Adults**

<b>IE Setting</b>	<b>Empiric Therapy<sup>1</sup></b>	<b>Alternate Empiric Therapy</b>	<b>Likely Pathogens</b>	<b>Directed Therapy</b>
Native valve	Penicillin G + gentamicin <i>OR</i> ceftriaxone	Vancomycin	Viridans streptococci <i>Streptococcus bovis</i> Enterococcus HACEK group <i>Staphylococcus aureus</i>	Penicillin G <sup>2</sup> or ceftriaxone <sup>3</sup> Penicillin G <sup>2</sup> or ceftriaxone <sup>3</sup> Ampicillin <sup>4</sup> + gentamicin <sup>5</sup> Ceftriaxone <sup>3</sup> Oxacillin ± gentamicin <sup>5,6</sup>
PVE	Vancomycin + gentamicin + rifampin	Same	<i>Staphylococcus aureus</i>  Coagulase-negative staphylococci Viridans streptococci  Enterococcus	Oxacillin + gentamicin + rifampin <sup>5,6</sup> Oxacillin + gentamicin + rifampin <sup>5,6</sup> Penicillin G <sup>7</sup> or ceftriaxone <sup>3</sup> ± gentamicin <sup>5</sup> Ampicillin <sup>4</sup> + gentamicin <sup>5</sup>

1 Antimicrobial therapy should be initiated AFTER blood cultures are drawn.

2 Penicillin MIC <0.12 mcg/mL = penicillin 12-18 million units/day in 4 or 6 divided doses (renal dose adjustment necessary).  
Penicillin MIC >0.12 mcg/mL and <0.5 mcg/mL = penicillin 24 million units/day in 4 or 6 divided doses (renal dose adjustment necessary).

Penicillin MIC >0.5 mcg/mL should be treated with enterococci regimen.

3 Ceftriaxone 2 g IV q24h.

4 Ampicillin 12 g/day in 6 divided doses (renal dose adjustment necessary). Vancomycin should be substituted for ampicillin-resistant isolates.

5 Low-dose gentamicin; 1 mg/kg IV q8h with interval adjusted for renal insufficiency.

6 Oxacillin 2 g IV q4h. Vancomycin should be substituted if the isolate is oxacillin-resistant.

7 Penicillin 24 million units/day in 4 or 6 divided doses (renal dose adjustment necessary).

**TABLE 8 Guidelines for Treatment of Bone and Joint Infections in Adults**

<b>Clinical Setting</b>	<b>Empiric Therapy</b>	<b>Likely Pathogens</b>	<b>Directed Therapy</b>	<b>Usual Duration<sup>1</sup></b>
<b>Osteomyelitis:</b>				
Healthy adult	Vancomycin	<i>Staphylococcus aureus</i>	Oxacillin or cefazolin <sup>2</sup>	4-6 wk
Posttraumatic	Piperacillin/ tazobactam + vancomycin	<i>Staphylococcus aureus</i> Streptococcus Gram-negative bacilli <i>Pseudomonas aeruginosa</i>	Oxacillin or cefazolin <sup>2</sup> Penicillin G or ampicillin Ceftriaxone Piperacillin/tazobactam	4-6 wk
Diabetic foot	Ampicillin/ sulbactam	Usually polymicrobial	Ampicillin/sulbactam	4-6 wk followed by PO
<b>Septic arthritis</b>	Vancomycin	<i>Staphylococcus aureus</i> Gonococcus <sup>3</sup>	Oxacillin or cefazolin <sup>2</sup> Ceftriaxone	4 wk 2 wk <sup>4</sup>
<b>Total joint replacement</b>	Vancomycin	<i>Staphylococcus aureus</i> <i>Staphylococcus epidermidis</i> Streptococcus	Oxacillin or cefazolin <sup>2</sup> Vancomycin <sup>5</sup> Penicillin G or ampicillin	4 wk

1 May require prolonged therapy, depending on clinical situation.

2 Substitute vancomycin if oxacillin-resistant.

3 Young adults.

4 May switch to oral therapy when clinically indicated.

5 Substitute oxacillin or cefazolin if susceptible.

**TABLE 9 Guidelines for Treatment of Urinary Tract Infections<sup>1</sup> in Adults**

<b>Clinical Setting</b>	<b>Likely Pathogens</b>	<b>Empiric Therapy</b>	<b>Alternatives</b>	<b>Usual Duration</b>
Acute uncomplicated cystitis	<i>Escherichia coli</i> , other Enterobacteriace	TMP/SMX <sup>2</sup>	Ciprofloxacin <sup>2</sup>	3 d
Mild-moderate pyelonephritis <sup>3</sup>	<i>Escherichia coli</i> , other Enterobacteriaceae	TMP/SMX <sup>2</sup>	Ciprofloxacin <sup>2</sup>	10-14 d
Severe pyelonephritis <sup>4</sup>	<i>Escherichia coli</i> , other Enterobacteriace	Piperacillin/tazobactam <sup>5,6</sup>	Ciprofloxacin <sup>5,6</sup>	10-14 d

1 UTI defined as symptoms plus pyuria (ie, >10 WBC).

2 Oral therapy preferred.

3 Limited nausea and vomiting; able to tolerate oral medication.

4 Nausea and vomiting; NPO.

5 May switch to oral therapy when appropriate.

6 Narrow therapy when culture and susceptibility results are available.



**TABLE 10 Guidelines for Treatment of Sexually Transmitted Infections**

Disease Pathogens	Recommended Treatment		Comments
	Primary	Alternates	
<b>Chancroid:</b> <i>Haemophilus ducreyi</i>	Erythromycin 500 mg PO tid × 7 d	Ceftriaxone 250 mg IM × 1 or azithromycin 1 g PO × 1	—
<b>Uncomplicated Gonorrhea</b> <i>Neisseria gonorrhoeae</i>	Ceftriaxone 250 mg IM × 1 dose	Azithromycin 1 g × 1 dose	—
<b>Disseminated gonorrhea:</b> <i>Neisseria gonorrhoeae</i>	Ceftriaxone 1 g IV q24h × 1-2 d or until improved, followed by cefixime <sup>1</sup> 400 mg PO bid to complete total therapy of 7-10 d		—
<b>Epididymitis (sexually acquired):</b> <i>Chlamydia trachomatis</i> <i>Neisseria gonorrhoeae</i>	Ceftriaxone 250 mg IM × 1 + doxycycline 100 mg PO bid × 10 d	Levofloxacin 500 mg PO × 10 d	Levofloxacin should only be used if nonsexually acquired epididymitis, due to FQ-resistant <i>N gonorrhoeae</i>

(Table continued on following page)

**TABLE 10 Guidelines for Treatment of Sexually Transmitted Infections** *(continued)*

Disease	Recommended Treatment		Comments
Pathogens	Primary	Alternates	
<b>Genital herpes:</b>			
Herpes simplex virus	First episode genital: Acyclovir 400 mg PO tid × 7-10 d First episode proctitis: Acyclovir 400 mg PO 5×/d × 7-10 d Severe herpes infection: Acyclovir 5 mg/kg IV q8h × 5-7 d		Recurrent: Acyclovir 400 mg PO tid or 800 mg PO bid × 5 d or 800 mg PO tid × 2 d Prevention of recurrence: Acyclovir 400 mg PO bid
<b>Pelvic inflammatory disease (PID):</b>			
<i>Chlamydia trachomatis</i> <i>Neisseria gonorrhoeae</i> <i>Mycoplasma hominis</i> Streptococci Enterobacteriaceae Anaerobes	Inpatient: Ceftriaxone 2 g IV q24h + doxycycline 100 mg IV q12h ± metronidazole 500 mg IV q12h until improved, then doxycycline 100 mg PO bid × 14 d Outpatient: Ceftriaxone 250 mg IM × 1 + doxycycline 100 mg PO bid ± metronidazole 500 mg PO bid × 14 d	Clindamycin 900 mg IV q8h + gentamicin, followed by doxycycline 100 mg PO bid to complete total therapy of 14 d	Refer to Table 18 for gentamicin dosing. Evaluate and treat sexual partners. Test for syphilis and HIV. Erythromycin stearate 500 mg PO qid instead of doxycycline if pregnant. For PID unrelated to sexual activity, treat as for intra-abdominal sepsis

*(Table continued on following page)*

**TABLE 10 Guidelines for Treatment of Sexually Transmitted Infections** *(continued)*

Disease Pathogens	Recommended Treatment		Comments
	Primary	Alternates	
<b>Syphilis:</b> <i>Treponema pallidum</i>	Primary, secondary or latent Penicillin G benzathine 2.4 million units IM × 1	<1 year: Doxycycline 100 mg PO bid × 14 d	All stages of syphilis require follow-up for possible relapse. Evaluate and treat sexual partners. Test for HIV. Pregnant women allergic to penicillin should be desensitized
	Late latent >1 year: Penicillin G benzathine 2.4 million units IM q wk × 3 wk	Doxycycline 100 mg PO bid × 28 d	
	Neurosyphilis: Penicillin G 3-4 million units IV q4h × 10-14 d	Procaine penicillin 2.4 million units IM q24h + Probenecid 500 mg PO qid × 10-14 d	Patient allergic to penicillin should be desensitized

*(Table continued on following page)*

**TABLE 10 Guidelines for Treatment of Sexually Transmitted Infections** *(continued)*

Disease Pathogens	Recommended Treatment Primary	Alternates	Comments
<b>Urethritis or cervicitis:</b>			
<i>Chlamydia trachomatis</i>	Ceftriaxone 250 mg IM	Azithromycin 2 g PO	Quinolones do not eradicate incubating syphilis. Evaluate and treat sexual partners. Test for syphilis and HIV. Due to increased prevalence of fluoroquinolone-resistant <i>Neisseria gonorrhoeae</i> the CDC no longer recommends fluoroquinolones for the treatment of gonorrhea
<i>Ureaplasma urealyticum</i>	× 1 + doxycycline	× 1	
<i>Neisseria gonorrhoeae</i>	100 mg PO bid × 7 d		

1 Ciprofloxacin may be used if susceptibility documented.

**TABLE 11 Guidelines for Treatment of Bacterial Meningitis in Adults**

<b>Clinical Setting</b>	<b>Empiric Therapy</b>	<b>Likely Pathogens</b>	<b>Directed Therapy</b>	<b>Usual Duration</b>
Community <sup>1</sup>	Vancomycin + ceftriaxone <sup>2</sup>	Pneumococcus Meningococcus <i>Haemophilus influenzae</i>	Penicillin G <sup>3</sup> Penicillin G Ceftriaxone <sup>2,4</sup>	2 wk 1-2 wk 1-2 wk
Immunocompromised or age >50 years	Ceftriaxone <sup>2</sup> + vancomycin + ampicillin	<i>Listeria</i> sp GNB ( <i>Pseudomonas aeruginosa</i> ) Pneumococcus	Ampicillin + gentamicin Ceftazidime <sup>6</sup> + gentamicin <sup>7</sup> Penicillin G <sup>3</sup>	2-3 wk <sup>5</sup>
Postneurosurgical/posttraumatic	Vancomycin + ceftazidime <sup>6</sup>	<i>Staphylococcus epidermidis</i> <i>Staphylococcus aureus</i> GNB ( <i>Pseudomonas aeruginosa</i> ) Pneumococcus	Vancomycin <sup>8</sup> Oxacillin <sup>9</sup> Ceftazidime <sup>6</sup> + gentamicin <sup>7</sup> Penicillin G <sup>3</sup>	2-4 wk

1 If age >50 years or immunocompromised, consider *Listeria* and add ampicillin.

2 Ceftriaxone 2 g IV q12h.

3 Substitute ceftriaxone or vancomycin if isolate is resistant to penicillin.

4 If isolate is  $\beta$ -lactamase-negative, ampicillin may be substituted.

5 Three weeks recommended for GNB.

6 Ceftazidime 2 g IV q8h (renal dose adjustment necessary).

7 Substitute tobramycin if resistant to gentamicin.

8 Substitute oxacillin if susceptible.

9 Substitute vancomycin if oxacillin-resistant.

## TABLE 12 Guidelines for Treatment of Febrile Neutropenia<sup>1</sup>

Clinically stable	Piperacillin/tazobactam 3.375 g IV q6h <sup>2</sup>
Pencillin allergy with history of: Rash Anaphylaxis	Ceftazidime 2 g IV q8h <sup>2</sup> Aztreonam 2 g IV q6h <sup>2</sup> + vancomycin <sup>3</sup> + gentamicin <sup>4</sup>
Severe mucositis <i>or</i> Suspected catheter-related infection <i>or</i> Suspected skin or skin structure infection <i>or</i> Gram-positive organism in blood cultures	Add vancomycin <sup>3,5</sup> to regimen
Clinically unstable (based on BP, HR, RR, and mental status)	Add gentamicin <sup>4</sup> and vancomycin <sup>3,5</sup> to regimen
Fever $\geq$ 72 hours on broad-spectrum antimicrobials	Consider adding voriconazole
Fever >72 hours and hemodynamic instability and/or respiratory distress	Consider change in antibacterial regimen (eg, change to meropenem)

1 Neutropenia ANC <500.

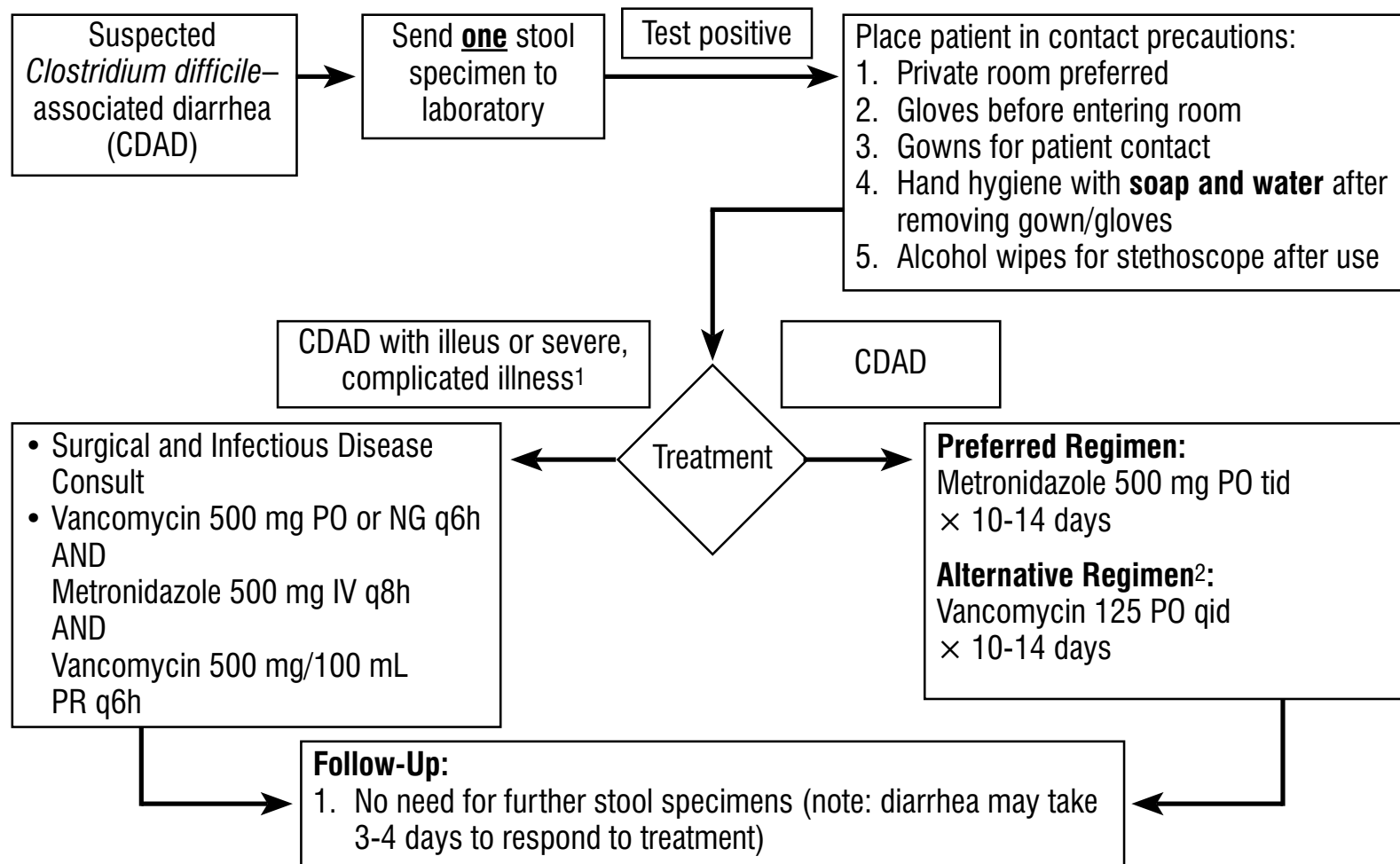
2 Renal dose adjustment necessary.

3 See Table 20 for dosing recommendations.

4 See Table 18 and Table 19 for dosing recommendations; extended interval dosing preferred if patient meets criteria.

5 Consider discontinuing vancomycin if cultures negative for MRSA at 48 hours.

**TABLE 13 Guidelines for Management of *Clostridium difficile* Toxin-Positive Diarrhea**



1 Severe, complicated illness defined as hypotension, shock, or ileus.

2 Consider vancomycin if metronidazole intolerant, failing to respond to metronidazole (ie, failure to improve after 3 to 4 days of therapy), or severe disease defined as WBC  $\geq 15,000$  or serum creatinine  $> 1.5 \times$  baseline.

## TABLE 14 Treatment of Skin and Skin Structure Infections<sup>1</sup>

Clinical Setting	Likely Pathogens	Empiric Therapy	Alternatives	Usual Duration
Uncomplicated cellulitis <sup>2</sup>	<i>S aureus</i> Streptococci	Oxacillin or cefazolin <sup>3</sup>	Vancomycin <sup>3,4</sup>	7 days
Diabetic foot	<i>S aureus</i> Streptococci Aerobic GNBs Anaerobes	Ampicillin/sulbactam	Ciprofloxacin + clindamycin	Guided by patient response to treatments
Necrotizing fasciitis	Group A streptococci Polymicrobial	STAT Surgery Consult Vancomycin + clindamycin		Guided by patient response to treatments

1 If abscess present, incision and drainage (I&D) is imperative for cure. I&D may be sufficient if isolated abscess <5 cm.

2 Complicating risk factors: chronic ulcer; including diabetic, vascular insufficiency; including chronic venous stasis and peripheral arterial disease, surgical wound, residence in health care facility within 90 days, recurrent cellulitis > twice in the preceding year, animal or human bite, indwelling medical device, perirectal infection, periorbital infection, salt or fresh water exposure, and immunocompromised state.

3 If culture negative or unavailable, change to oral doxycycline 100 mg PO bid, TMP/SMX DS 1-2 tabs PO bid, or clindamycin 300-450 mg PO tid when able.

4 Use first-line empiric if MRSA risk factors present. Risk factors include: injection drug use, diabetes mellitus, end-stage renal disease, human immunodeficiency virus infection, contact sports, prisoners, soldiers, men who have sex with men, Native Americans, recent antibiotic exposure, known colonization with MRSA, contact with person diagnosed with MRSA infection, and report of spider bite.



## TABLE 15 Guidelines for Antimicrobial Dosing in Adults

Drug	Admin Route	CrCl (mL/min)	Suggested Dosage Regimen	Supplement for Dialysis	
				H/D <sup>1</sup>	P/D
Acyclovir	IV/PO	>50	5-10 mg/kg q8h	Yes	—
		25-50	5-10 mg/kg q12h		
		10-25	5-10 mg/kg q24h		
		0-10	2.5-5 mg/kg q24h		
Amantadine	PO	>80	100 mg bid	No	No
		60-80	200 mg/100 mg, alternating q24h		
		40-60	100 mg q24h		
		30-40	200 mg 2×/wk		
		20-30	100 mg 3×/wk		
		10-20	200 mg/100 mg, alternating weekly		
Amikacin	IV/IM	Individualize regimen with serum concentrations (see Table 18)			
Amoxicillin	PO	>50	250-500 mg q8h	Yes	No
		10-50	250-500 mg q8-12h		
		<10	250-500 mg q12h		
Amoxicillin/ clavulanate	PO	>30	875 mg q12h OR 250-500 mg q8h	Yes	No
		10-30	250-500 mg q12h		
		<10	250-500 mg q24h		
Amphotericin B	IV	No renal dosage adjustment necessary	0.5-1 mg/kg q24h (max dose 100 mg)	No	No
Amphotericin B Lipid Complex ABELCET®	IV	See Table 16 for appropriate usage guidelines			
Ampicillin	IV	>50	1-2 g q4-6h	Yes	No
		10-50	1-2 g q6-12h		
		<10	1-2 g q8-12h		

(Table continued on following page)

**TABLE 15 Guidelines for Antimicrobial Dosing in Adults** *(continued)*

Drug	Admin Route	CrCl (mL/min)	Suggested Dosage Regimen	Supplement for Dialysis	
				H/D <sup>1</sup>	P/D
Ampicillin/sulbactam	IV	>30	1.5-3 g q6-8h	Yes	—
		15-30	1.5-3 g q12h		
		<15	1.5-3 g q24h		
Atovaquone	PO	No renal dose adjustment necessary	750 mg bid	—	—
Atovaquone/proguanil <sup>2</sup>	PO	No renal dose adjustment necessary	1 g/400 mg q24h	—	—
Azithromycin	IV	No renal dose adjustment necessary	500 mg q24h	No	No
	PO	No renal dose adjustment necessary	250-500 mg q24h	No	No
Aztreonam	IV	See Table 16 for appropriate usage guidelines			
Cefazolin <sup>3</sup>	IV	>55	1 g q8h	Yes	No
		35-54	1 g q8-12h		
		11-34	500 mg-1 g q12h		
		<10	500 mg-1 g q24h		
Cefdinir	PO	>30	300 mg q12h or 600 mg q24h	Yes	—
		<30	300 mg q24h		
Cefixime <sup>4</sup>	PO	>60	400 mg q24h	Yes	—
		21-59	300 mg q24h		
		<20	200 mg q24h		
Cefpodoxime	PO	>30	100-400 mg q12h	No	—
		10-29	100-400 mg q24h		
		<10	100-400 mg 3×/wk		
Cefprozil	PO	>30	500 mg q12-24h	Yes	—
		<30	250 mg q12h		

*(Table continued on following page)*

**TABLE 15 Guidelines for Antimicrobial Dosing in Adults** *(continued)*

Drug	Admin Route	CrCl (mL/min)	Suggested Dosage Regimen	Supplement for Dialysis	
				H/D <sup>1</sup>	P/D
Ceftazidime	IV	See Table 16 for appropriate usage guidelines			
Ceftriaxone	IV	See Table 16 for appropriate usage guidelines			
Cefuroxime	IV	>20	750 mg-1.5 g q8-12h	Yes	No
		10-20	750 mg q12h		
		<10	750 mg q24h		
Cephalexin	PO	>40	250-500 mg q6h	Yes	Yes
		10-40	250-500 mg q8-12h		
		<10	250 mg q12-24h		
Chloramphenicol	IV	No renal dose adjustment necessary	0.5-1 g q6h	No	No
Cidofovir	IV	See Table 16 for appropriate usage guidelines			
Ciprofloxacin	IV	>30	400 mg q12h	No	—
		<30	400 mg q24h		
	PO	>30	250, 500 or 750 mg q12h	No	—
		<30	500 or 750 mg q24h		
Clarithromycin	PO	>30	250-500 mg q12h	—	—
		<30	250-500 mg q24h		
Clindamycin	IV	No renal dose adjustment necessary	600-900 mg q8h	No	No
	PO	No renal dose adjustment necessary	150-450 mg q6h	No	No
Clofazimine	PO	No renal dose adjustment necessary	100 mg q24h	—	—
Colistimethate	Inhaled	See Table 16 for appropriate usage guidelines			
	IV				

*(Table continued on following page)*

**TABLE 15 Guidelines for Antimicrobial Dosing in Adults** *(continued)*

Drug	Admin Route	CrCl (mL/min)	Suggested Dosage Regimen	Supplement for Dialysis	
				H/D <sup>1</sup>	P/D
Cytomegalovirus immune globulin	IV	See Table 16 for appropriate usage guidelines			
Dapsone	PO	No renal dose adjustment necessary	100 mg q24h	—	—
Daptomycin	IV	See Table 16 for appropriate usage guidelines			
Dicloxacillin	PO	No renal dose adjustment necessary	500 mg q6h	No	—
Doxycycline	IV/PO	No renal dose adjustment necessary	100 mg q12h	No	—
Erythromycin	IV	>10	0.5-1 g q6h	No	No
	PO	<10 No renal dose adjustment necessary	250-500 mg q6h 250-500 mg q6h	No	No
Ethambutol	PO	>50	15-25 mg/kg q24h	Yes	Yes
		10-50	15 mg/kg q24-36h		
		<10	15 mg/kg q48h Maximum daily dose: 2.5 g		
Fluconazole	IV/PO	>50	100-400 mg q24h	Yes	—
		10-50	50% of recommended dose		
Flucytosine	PO	>40	12.5-37.5 mg/kg q6h	Yes	—
		20-40	12.5-37.5 mg/kg q12h		
		10-20	12.5-37.5 mg/kg q24h		
		<10	12.5-37.5 mg/kg q24-48h		
Foscarnet	IV	See footnote 5 for dosing			
Fosfomycin	PO	No renal dose adjustment necessary	3 g × 1 dose (may be repeated if needed)		

*(Table continued on following page)*

**TABLE 15 Guidelines for Antimicrobial Dosing in Adults** *(continued)*

Drug	Admin Route	CrCl (mL/min)	Suggested Dosage Regimen	Supplement for Dialysis	
				H/D <sup>1</sup>	P/D
Ganciclovir	IV	>70	5 mg/kg q12h	Yes	—
		50-69	2.5 mg/kg q12h		
		25-49	2.5 mg/kg q24h		
		10-24	1.25 mg/kg q24h		
		<10	1.25 mg/kg 3×/wk, following hemodialysis		
Gentamicin	IM/IV	Individualize regimen with serum concentrations (see Table 18)			
Isoniazid	IV/PO	No renal dose adjustment necessary	300 mg q24h	Yes	Yes
Itraconazole	PO	No renal dose adjustment necessary	200 mg q12-24h	No	No
Ketoconazole	PO	No renal dose adjustment necessary	200 mg q24h	No	No
Levofloxacin	IV/PO	See Table 16 for appropriate usage guidelines			
Linezolid	IV/PO	See Table 16 for appropriate usage guidelines			
Meropenem	IV	See Table 16 for appropriate usage guidelines			
Metronidazole	PO/IV	>10	500 mg q6-8h	Yes	—
		<10	500 mg q8-12h		
Micafungin	IV	See Table 16 for appropriate usage guidelines			
Nitrofurantoin	PO	>50	50-100 mg q6h	—	—
		<50	Avoid use		
Norfloxacin	PO	>30	400 mg q12h	No	—
		<30	400 mg q24h		
Oxacillin	IV	No renal dose adjustment necessary	1-2 g q4-6h	No	—

*(Table continued on following page)*

**TABLE 15 Guidelines for Antimicrobial Dosing in Adults** *(continued)*

Drug	Admin Route	CrCl (mL/min)	Suggested Dosage Regimen	Supplement for Dialysis	
				H/D <sup>1</sup>	P/D
Oseltamivir	PO	>30 10-30 <10	75 mg bid 75 mg q24h 30 mg, following hemodialysis		
Penicillin G	IV	>50 10-50 <10	2-4 million units q2-4h 1-2 million units q4-6h 1-2 million units q8-12h OR 0.5-1 million units q4-6h	Yes	—
Penicillin VK	PO	>10 <10	250-500 mg q6h 250 mg q6h	Yes	—
Pentamidine	IV	>50 10-50 <10	4 mg/kg q24h 4 mg/kg q24-36h 4 mg/kg q48h	—	—
Piperacillin/ tazobactam	IV	>40 20-40 <20	3.375 g q6h 3.375 g q8h 3.375 g q12h	Yes	—
Posaconazole	PO	See Table 16 for appropriate usage guidelines			
Pyrazinamide	PO	No renal dose adjustment necessary	15-30 mg/kg q24h Maximum dose: 2 g	—	—
Pyrimethamine	PO <sup>6</sup>	No renal dose adjustment necessary	100 mg q24h	—	—
Quinupristin/ dalfopristin	IV	See Table 16 for appropriate usage guidelines			
Rifabutin	PO	No renal dose adjustment necessary	300 mg q24h	—	—

*(Table continued on following page)*

**TABLE 15 Guidelines for Antimicrobial Dosing in Adults** *(continued)*

Drug	Admin Route	CrCl (mL/min)	Suggested Dosage Regimen	Supplement for Dialysis	
				H/D <sup>1</sup>	P/D
Rifampin	IV/PO	No renal dose adjustment necessary	600 mg q24h	No	—
Rimantadine	PO	>10 <10	100 mg bid 100 mg q24h	—	—
Streptomycin <sup>7</sup>	IV/IM	>50 10-50 <10	7.5 mg/kg q12h 7.5 mg/kg q24-72h 7.5 mg/kg q72-96h	Yes	Yes
Sulfisoxazole	PO	>50 10-50 <10	1-2 g q6h 1 g q8-12h 1 g q12-24h	Yes	No
Sulfadiazine	PO	No renal dose adjustment necessary	1-2 g q6h	—	—
Tetracycline	PO	>50 10-50 <10	250-500 mg q6-12h 250-500 mg q12-24h 250-500 mg q24h	No	No
Tigecycline	IV	See Table 16 for appropriate usage guidelines			
Tobramycin	IV/IM	Individualize dosing with serum concentrations (see Table 18)			
Trimethoprim/ sulfamethoxazole	IV	>30 15-30 <15	5 mg/kg q6-8h 2.5-5 mg/kg q12h 2.5-5 mg/kg q24h (All doses based on trimethoprim)	Yes	No
	PO <sup>8</sup>	>30 <30	1 DS q12h 1 DS q24h 1 DS = 160 mg of trimethoprim	Yes	No

*(Table continued on following page)*

**TABLE 15 Guidelines for Antimicrobial Dosing in Adults** *(continued)*

Drug	Admin Route	CrCl (mL/min)	Suggested Dosage Regimen	Supplement for Dialysis	
				H/D <sup>1</sup>	P/D
Trimethoprim	PO	>50	100-200 mg q6h 10-50 <10	Yes 100 mg q12-24h 50-100 mg q24h	—
Valganciclovir	PO	See Table 16 for appropriate usage guidelines			
Vancomycin	IV	See Table 20 for individualized dosing			
	PO	No renal dose adjustment necessary	125 mg q6h	No	No
Voriconazole	IV/PO	See Table 16 for appropriate usage guidelines			

1 Assure that full daily dosing occurs after dialysis as an alternative to supplemental dosing.

2 For malaria prophylaxis, the recommended dose is 250/100 mg q24h.

3 Dose may be doubled in severe infection.

4 Only available in a 100 mg/5 mL oral suspension.

5 Foscarnet dosing in renal insufficiency:

Creatinine Clearance mL/min/kg	Induction for HSV (dose in mg/kg) Equivalent to 40 mg/kg q12h	Induction for CMV (dose in mg/kg) Equivalent to 90 mg/kg q12h	Maintenance Dosage for CMV (dose in mg/kg) Equivalent to 90 mg/kg q24h
	>1.4	40 q12h	90 q12h
>1-1.4	30 q12h	70 q12h	70 q24h
>0.8-1	20 q12h	50 q12h	50 q24h
>0.6-0.8	35 q24h	80 q24h	80 q48h
>0.5-0.6	25 q24h	60 q24h	60 q48h
≥0.4-0.5	20 q24h	50 q24h	50 q48h
<0.4	Not recommended	Not recommended	Not recommended

6 Plus folinic acid, 10 mg, with each dose of pyrimethamine.

7 Recommended dosing for synergy in the treatment of enterococcal infections. Serum levels should be monitored.

8 Higher doses may be warranted for serious infections; up to 3 DS q8h or 2 DS q6h.



**TABLE 16 Formulary-Approved Indications and Dosing of Restricted Antimicrobial Agents in Adults**

<b>Drug/ Indication</b>	<b>Admin Route</b>	<b>Usual Regimen</b>	<b>~Cost/d</b>	<b>~Cost/wk</b>	<b>CrCl (mL/min)</b>	<b>Suggested Dosage Regimen</b>	<b>Supplement for Dialysis H/D P/D</b>	
Amphotericin B Lipid Complex ABELCET®	IV	Prophylaxis: 3 mg/kg q24h	\$150	\$1050	—	No renal dose adjustment necessary		
• Infectious Diseases Service only		Treatment: 5 mg/kg q24h	\$260	\$1820				
• Serum creatinine >2 <sup>1</sup> or 50% decrease in baseline renal function								
• Amphotericin B failure								
Aztreonam	IV	1-2 g q6-8h	\$100-300	\$700-2100	>30	1-2 g q6-8h	Yes	Yes
• Infections due to resistant organisms					10-30	1-500 mg q6-8h		
• Allergy to β-lactam antimicrobials					<10	250-500 mg q6-8h		
Ceftazidime	IV	1-2 g q8h	\$20-45	\$140-315	>50	1-2 g q8h	Yes	Yes
• Penicillin-allergic patients who can tolerate cephalosporins					31-50	1-2 g q12h		
• Organisms resistant to piperacillin/tazobactam					16-30	1-2 g q24h		
• Failed empiric piperacillin/tazobactam therapy					<15	500 mg-1g q24h		
• Neurosurgical patients								
• Gram-negative monotherapy in febrile neutropenic patients								
Ceftriaxone	IM/IV	1 g q24h	\$10	\$70	—	No renal dose adjustment necessary		
• Dose limited to 1 g q24h unless endocarditis or meningitis								

*(Table continued on following page)*

**TABLE 16** Formulary-Approved Indications and Dosing of Restricted Antimicrobial Agents in Adults *(continued)*

Drug/ Indication	Admin Route	Usual Regimen	~Cost/d	~Cost/wk	CrCl (mL/min)	Suggested Dosage Regimen	Supplement for Dialysis	
							H/D	P/D
Cidofovir <sup>2</sup> • Infectious Diseases Service only	IV	5 mg/kg every other week (+ probenecid and hydration)	N/A	\$297	<55	Avoid use	—	—
Colistimethate • Infectious Diseases Service only	Inhaled	75 mg q12h	Inhaled: \$15	Inhaled: \$105				
• Infectious Diseases Services only • Dose based on ideal body weight • Optional 3 mg/kg loading dose	IV	1.5 mg/kg q8h	\$50	\$350	≥30 10-30 <10 or dialysis	1.5 mg/kg q8h 1.25 mg/kg q12h 1.5 mg/kg q24h	No	No
Cytomegalovirus immune globulin • Infectious Diseases and Transplant Services	IV	Initial dose: 150 mg/kg Week 2, 4, 6, 8: 100 mg/kg Week 12, 16: 50 mg/kg Cost/course: ~\$12,000			—	No renal dose adjustment necessary		

*(Table continued on following page)*

**TABLE 16 Formulary-Approved Indications and Dosing of Restricted Antimicrobial Agents in Adults** *(continued)*

Drug/ Indication	Admin Route	Usual Regimen	~Cost		CrCl (mL/min)	Suggested Dosage Regimen	Supplement for Dialysis	
			~Cost/d	~Cost/wk			H/D	P/D
Daptomycin • Infectious Diseases Service only • Not indicated for pneumonia • Higher mg/kg doses may be warranted for certain infections	IV	6 mg/kg q24h	\$200 (500 mg q24h)	\$1400	≥30 <30	q24h q48h	—	—
Ertapenem • Infectious Diseases Service • Single dose prior to discharge for CoPAT	IV	1 g q24h	\$50	\$350	≥30 <30	1 g q24h 500 mg q24h	—	—
Levofloxacin • Penicillin- allergic patients with CAP	IV/PO	750 mg q24h	IV: \$20 PO: \$1	\$140 \$7	≥50 20-49 ≤19	750 mg q24h 750 mg q48h 750 mg x 1 then 500 mg q48h	—	—
Linezolid • Infectious Diseases Service only	IV/PO	600 mg q12h	IV: \$180 PO: \$140	\$1260 \$980	—	No renal dose adjustment necessary		

*(Table continued on following page)*

**TABLE 16 Formulary-Approved Indications and Dosing of Restricted Antimicrobial Agents in Adults** *(continued)*

Drug/ Indication	Admin Route	Usual Regimen	~Cost/d	~Cost/wk	CrCl (mL/min)	Suggested Dosage Regimen	Supplement for Dialysis	
							H/D	P/D
Meropenem	IV	500 mg q6h	\$40	\$300	≥50	500 mg q6h or 1 g q8h	Yes	—
<ul style="list-style-type: none"> <li>Infections due to Pip/Tazo-resistant organisms or Pip/Tazo clinical failures</li> <li>Dose may be increased for CNS infection</li> </ul>					26-49	500 mg q8h or 1 g q12h		
					10-25	500 mg q12h		
					<10	500 mg q24h		
Micafungin	IV	100 mg q24h	\$80	\$560	—	No renal dose adjustment necessary		
<ul style="list-style-type: none"> <li>Infectious Diseases Service only</li> <li>100-mg dose recommended for candidemia, disseminated candidiasis, candida peritonitis, and abscesses</li> <li>150-mg dose recommended for candida endocarditis, osteomyelitis, or meningitis and mould infections</li> </ul>		150 mg q24h	\$120	\$840				
Posaconazole	PO	200 mg q8h	\$90	\$630	—	No renal dose adjustment necessary		
<ul style="list-style-type: none"> <li>Infectious Diseases Service</li> <li>BMT Service</li> </ul>		200 mg q6h	\$120	\$840				
Quinupristin/ dalfopristin	IV	7.5 mg/kg q8-12h	\$500	\$3500	—	No renal dose adjustment necessary		
<ul style="list-style-type: none"> <li>Infectious Diseases Services only</li> </ul>			(500 mg q8h)					

*(Table continued on following page)*

**TABLE 16 Formulary-Approved Indications and Dosing of Restricted Antimicrobial Agents in Adults** *(continued)*

Drug/ Indication	Admin Route	Usual Regimen	~Cost/d	~Cost/wk	CrCl (mL/min)	Suggested Dosage Regimen	Supplement for Dialysis	
							H/D	P/D
Tigecycline	IV	Loading dose: 100 mg × 1	\$115		—	No renal dose adjustment necessary		
• Infectious Diseases Service only		Maintenance dose: 50 mg q12h	\$115	\$805				
• Treatment of MDR Gram-negative infections								
Valganciclovir	PO	900 mg bid	\$100	\$700	(See table below)	Yes	—	
• Infectious Diseases Service								
• Transplantation services:		CrCl (mL/min)		Induction		Maintenance		
		≥60		900 mg q12h		900 mg q24h		
		40-59		450 mg q12h		450 mg q24h		
		25-39		450 mg q24h		450 mg q48h		
		10-24		450 mg q48h		450 mg q2×/wk		
		<10		Not recommended		Not recommended		
Voriconazole	IV/PO	Loading dose: 400 mg q12h × 2 doses	IV: \$430	—	—	No renal dosage adjustment necessary; IV not recommended in patients with a CrCl <50 mL/min		
• Infectious Diseases Service		(>100 kg; 600 mg q12h × 2 doses)	PO: \$160					
• Hematology/Oncology Service		Maintenance dose: 200 mg q12h	IV: \$215	IV: \$1505				
			PO: \$80	PO: \$560				

1 Not for chronic renal failure.

2 Administer with probenecid; 2 g orally 3 hours prior to each infusion and 1 g at 2 and 8 hours after completion of infusion (total 4 g). Hydrate with 1 L of 0.9% NS IV prior to infusion. A second liter may be given over 1 to 3 hour period immediately following infusion, if tolerated.

# TABLE 17 Antiretrovirals<sup>1</sup>

(Guidelines subject to change; check [www.aidsinfo.nih.gov](http://www.aidsinfo.nih.gov) for updates.)

<b>Generic: Chemical (Trade) Drug Names Manufacturer</b>	<b>Dosage Forms</b>	<b>Recommended Dose &amp; Dosage Adjustments</b>	<b>Selected Adverse Reactions</b>
<b>Entry Inhibitor</b>			
Maraviroc (Selzentry) Pfizer	Tab: 150, 300 mg	300 mg bid 150 mg bid when given with PIs other than tipranavir 600 mg bid when given with efavirenz, rifampin, or etravirine	Hepatotoxicity, rash, upper respiratory infection, postural hypotension  Avoid use with CrCl <30 mL/min if used with strong inhibitor or inducer Tropism testing required prior to use
<b>Integrase Inhibitor</b>			
Raltegravir (Isentress) Merck	Tab: 400 mg	400 mg bid	GI upset, headache, fatigue, hyperglyce- mia, creatine kinase elevations
<b>Nucleoside Reverse Transcriptase Inhibitors<sup>2</sup></b>			
Abacavir (Ziagen) <sup>3</sup> GlaxoSmithKline	Tab: 300 mg Oral Sol: 20 mg/mL, 240 mL/bottle	300 mg bid 600 mg daily Child-Pugh: 5-6: 200 mg bid >6: contraindicated	Hypersensitivity syndrome (fever, fatigue, GI symptoms, ± rash). DO NOT RESTART: screen for HLAB*5701 prior to use
Didanosine Delayed- Release (Videx EC) Bristol-Myers Squibb	Cap: 125, 200, 250, 400 mg Ped Powder: 2, 4 g	≥60 kg: 400 mg q24h on empty stomach <60 kg: 250 mg q24h Adjust for CrCl <60 mL/min Dosing for persons on concomitant tenofovir: 60 kg: 250 mg daily <60 kg: 200 mg daily	Pancreatitis, peripheral neuropathy, nausea, potential association with noncirrhotic portal hypertension, presenting with esophageal varices Insulin resistance/diabetes

(Table continued on following page)

**TABLE 17 Antiretrovirals<sup>1</sup>** *(continued)*

<b>Generic: Chemical (Trade) Drug Names Manufacturer</b>	<b>Dosage Forms</b>	<b>Recommended Dose &amp; Dosage Adjustments</b>	<b>Selected Adverse Reactions</b>
<b>Nucleoside Reverse Transcriptase Inhibitors<sup>2</sup></b>			
Emtricitabine: FTC <sup>3</sup> (Emtriva) Gilead	Cap: 200 mg  Oral Sol: 10 mg/mL, 170 mL/bottle	200 mg q24h CrCl (mL/min): 30-49: 200 mg q48h 15-29: 200 mg q72h <15: 200 mg q96h  240 mg q24h CrCl (mL/min): 30-49: 120 mg q24h 15-29: 80 mg q24h <15: 60 mg q24h	Nausea, diarrhea, headache, rash, hyperpigmentation/skin discoloration
Lamivudine: 3TC (Epivir) <sup>3</sup> GlaxoSmithKline	Tab: 150, 300 mg Oral Sol: 10 mg/mL, 240 mL/bottle	≥50 kg: 150 mg bid; 300 mg q24h <50 kg: 2 mg/kg bid CrCl (mL/min): 30-49: 150 mg q24h 15-29: 150 mg × 1, then 100 mg q24h 5-14: 150 mg × 1, then 50 mg q24h <5: 50 mg × 1, then 25 mg q24h	Minimal toxicity, pancreatitis in children
Stavudine: d4T (Zerit) Bristol-Myers Squibb	Cap: 15, 20, 30, 40 mg Oral Sol: 1 mg/mL, 200 mL/bottle	≥60 kg: 40 mg bid CrCl (mL/min): 26-50: 20 mg bid 10-25: 20 mg q24h <60 kg: 30 mg bid CrCl (mL/min): 26-50: 15 mg bid 10-25: 15 mg q24h	Peripheral neuropathy, headache, abdominal or back pain, asthenia, nausea, diarrhea, myalgia, pancreatitis, mitochondrial toxicities

*(Table continued on following page)*

**TABLE 17 Antiretrovirals<sup>1</sup>** *(continued)*

<b>Generic: Chemical (Trade) Drug Names Manufacturer</b>	<b>Dosage Forms</b>	<b>Recommended Dose &amp; Dosage Adjustments</b>	<b>Selected Adverse Reactions</b>
<b>Nucleoside Reverse Transcriptase Inhibitors<sup>2</sup></b>			
Zidovudine: AZT (Retrovir) <sup>3</sup> GlaxoSmithKline	Tab: 300 mg Cap: 100 mg Syrup: 50 mg/5 mL, 240 mL/bottle Inj: 10 mg/mL, 20 mL/vial	200 mg tid or 300 mg bid on empty stomach CrCl (mL/min): <15: 100 mg tid or 300 mg daily	Anemia, neutropenia, thrombocytopenia, headache, nausea, vomiting, myopathy, hepatitis, hyperpigmentation of nails
<b>Nucleotide Reverse Transcriptase Inhibitors<sup>2</sup></b>			
Tenofovir (Viread) <sup>3</sup> Gilead	Tab: 300 mg	CrCl (mL/min): ≥50: 300 mg q24h with food 30-49: 300 mg q48h with food 10-29: 300 mg twice weekly with food Dialysis: 300 mg weekly	Asthenia, headache, diarrhea, nausea, Fanconi syndrome, osteomalacia
<b>Non-nucleoside Reverse Transcriptase Inhibitors</b>			
Efavirenz (Sustiva) <sup>3</sup> Bristol-Myers Squibb	Cap: 50, 200 mg Tab: 600 mg	600 mg q24h	Dizziness, confusion, hallucinations, rash, psychiatric symptoms, vivid dreams, hyperlipidemia
Etravirine (Intelence) Tibotec	Tab: 200 mg	200 mg bid after a meal	Rash, nausea, hypersensitivity reactions
Nevirapine (Viramune, Viramune XR) Roxane	Tab: 200 mg Oral Susp: 10 mg/mL, 240 mL/bottle Tab (XR): 400 mg	200 mg q24h × 14 d, then 200 mg bid or 400 mg (XR) q24h	Rash, abnormal liver function tests, hepatotoxicity. Use with caution in men with CD4 >400 and women >250 due to increased risk of hepatotoxicity

*(Table continued on following page)*



**TABLE 17 Antiretrovirals<sup>1</sup>** *(continued)*

Generic: Chemical (Trade) Drug Names Manufacturer	Dosage Forms	Recommended Dose & Dosage Adjustments	Selected Adverse Reactions
<b>Protease Inhibitors<sup>4</sup></b>			
Atazanavir (Reyataz) Bristol-Myers Squibb	Cap: 100, 150, 200, 300 mg	<u>ARV-naïve:</u> 300/100 mg <sup>7</sup> q24h or 400 mg q24h <u>With TDF or AFV-experienced:</u> 300/100 mg q24h <sup>7</sup> <u>With EFV in ARV-naïve:</u> 400/100 mg <sup>7</sup> q24h <u>With DRV/RTV:</u> 300 mg q24h Do not use with ETR or NVP or in ARV-experienced patients on EFV Child-Pugh: 7-9: 300 mg q24h >9: Not recommended Not recommended for patients on hemodialysis	Rash, serum transaminase elevations, hyperlipidemia
Darunavir (Prezista) Ortho Biotech	Tab: 75, 150, 400, 600 mg	600/100 mg bid <sup>7</sup> 800/100 mg q24h <sup>5,7</sup>	Use with caution in patients with sulfonamide allergies, may cause hepatitis, rash

*(Table continued on following page)*

**TABLE 17 Antiretrovirals<sup>1</sup> (continued)**

<b>Generic: Chemical (Trade) Drug Names Manufacturer</b>	<b>Dosage Forms</b>	<b>Recommended Dose &amp; Dosage Adjustments</b>	<b>Selected Adverse Reactions</b>
<b>Protease Inhibitors<sup>4</sup></b>			
Fosamprenavir (Lexiva) GlaxoSmithKline	Tab: 700 mg  Oral Sol: 50 mg/mL	1400 mg bid <sup>6</sup> 700/100 mg bid <sup>7</sup> 1400/100 q24h <sup>6,7</sup> 1400/200 mg q24h <sup>6,7</sup> Child-Pugh: 5-6: 700 mg bid <sup>6</sup> 700 mg bid + RTV 100 mg daily 7-9: 700 mg bid <sup>6</sup> 450 mg bid + RTV 100 md daily 10-12: 350 mg bid <sup>6</sup> or 300/100 mg q24h	Rash, nausea, vomiting, diarrhea. Avoid boosted dose in persons with hepatic insufficiency
Indinavir (Crixivan) Merck	Cap: 100, 200, 400 mg	800 mg q8h with water <sup>8</sup> (hepatic insufficiency: 600 mg tid) 800/100 mg bid <sup>7</sup> 800/200 mg bid <sup>7</sup>	Hyperbilirubinemia, nephrolithiasis, abdominal pain, nausea, diarrhea, taste perversion
Lopinavir/ritonavir (Kaletra) Abbott	Tab: 100/25, 200/50 mg  Oral Sol: 80/20 mg/mL, 160 mL/bottle	400/100 mg bid <sup>6,7</sup> 800/200 mg q24h <sup>6,7,9</sup> 500/125 mg q24h <sup>10</sup>	Diarrhea, nausea, vomiting, abdominal pain, asthenia, headache. See ritonavir
Nelfinavir (Viracept) Agouron (Pfizer)	Tab: 250, 625 mg Oral Powder: 50 mg/g, 144 g/bottle	750 mg tid with food or 1250 mg bid	Diarrhea, nausea

*(Table continued on following page)*

**TABLE 17 Antiretrovirals<sup>1</sup>** *(continued)*

<b>Generic: Chemical (Trade) Drug Names Manufacturer</b>	<b>Dosage Forms</b>	<b>Recommended Dose &amp; Dosage Adjustments</b>	<b>Selected Adverse Reactions</b>
<b>Protease Inhibitors<sup>4</sup></b>			
Ritonavir (Norvir) Abbott	Tab: 100 mg Cap: 100 mg Oral Sol: 80 mg/mL, 240 mL/bottle	100-400 mg q12-24h with other protease inhibitor	Asthenia, nausea, diarrhea, vomiting, abdominal pain, circumoral and peripheral paresthesias, taste perversion
Saquinavir (Invirase) Roche	Cap: 200 mg Tab: 500 mg	1000/100 mg bid <sup>7</sup>	Diarrhea, abdominal discomfort, nausea, headache, PR and QT prolongation, torsades de pointes
Tipranavir (Aptivus) Boehringer Ingelheim	Cap: 250 mg Oral Sol: 100 mg/mL	500/200 mg <sup>7</sup> bid with food	Nausea, vomiting, diarrhea, rash, hepatotoxicity, intracranial hemorrhage. Use caution in those with chronic hepatitis B or C, sulfa allergies, and in those with moderate hepatic insufficiency
<b>Fusion Inhibitors</b>			
Enfuvirtide: T-20 (Fuzeon) Roche	Vials for injection: 90 mg/1 mL	90 mg SC q12h	Injection site reactions, pneumonia
<b>Combination Products</b>			
Abacavir/lamivudine (Epzicom) GlaxoSmithKline	Tab: 600/300 mg	1 tablet daily	Avoid in patients with hepatic impairment or CrCl <50 mL/min
Abacavir/lamivudine/ zidovudine (Trizivir) GlaxoSmithKline	Tab: 300/150/300 mg	1 tablet bid	Avoid in patients with CrCl <50 mL/min

*(Table continued on following page)*

**TABLE 17 Antiretrovirals<sup>1</sup>** (continued)

<b>Generic: Chemical (Trade) Drug Names Manufacturer</b>	<b>Dosage Forms</b>	<b>Recommended Dose &amp; Dosage Adjustments</b>	<b>Selected Adverse Reactions</b>
<b>Combination Products</b>			
Efavirenz/emtricitabine/ tenofovir (Atripla) Bristol-Myers Squibb/Gilead	Tab: 600/200/300 mg	1 tablet daily; not for patients with CrCl <50 mL/min	Avoid in patients with CrCl <50 mL/min
Emtricitabine/tenofovir (Truvada) Gilead	Tab: 200/300 mg	1 tablet daily CrCl (mL/min): 30-49: 1 tablet q48h	Avoid in patients with CrCl <30 mL/min
Lamivudine/zidovudine: 3TC/AZT (Combivir) GlaxoSmithKline	Tab: 150 mg/300 mg	1 tablet bid	Avoid in patients with CrCl <50 mL/min

- 1 These agents, especially protease inhibitors and non-nucleoside reverse transcriptase inhibitors, have numerous drug interactions. Please be aware of potential drug interactions when initiating or discontinuing any medication.
- 2 Therapy with these agents has been reported to cause lactic acidosis.
- 3 Available in combination product. See *Combination Products* section.
- 4 These agents have been associated with hyperglycemia, hypertriglyceridemia, fat redistribution, and possible increased bleeding episodes in patients with hemophilia.
- 5 Dose for ARV-naïve or -experienced patient with no darunavir mutations.
- 6 Only for treatment-naïve patients.
- 7 All boosted regimens utilize ritonavir. Boosted doses are listed as original protease inhibitor dose/ritonavir dose.
- 8 A minimum of 1.5 liters (48 ounces) of liquids per day is recommended.
- 9 Not for ≥3 LPV mutations, pregnant females, patients receiving EFV, NVP, FPV, NFV, carbamazepine, phenobarbital, or phenytoin.
- 10 Dose when given with EFV or NFV.

# TABLE 18 Traditional Aminoglycoside Dosing

Age	Serum Creatinine					
	0.8	1.0	1.2	1.5	2.0	>2.0
30	q8h	q8h	q8h	q12h	q24h	one dose
40	q8h	q12h	q12h	q24h	q24h	one dose
50	q12h	q12h	q12h	q24h	q24h	one dose
60	q12h	q12h	q12h	q24h	one dose	one dose
70	q24h	q24h	q24h	one dose	one dose	one dose
80	q24h	q24h	q24h	one dose	one dose	one dose
90	q24h	q24h	q24h	one dose	one dose	one dose

Dosing Interval	Dose (mg/kg)		Levels
	Tobramycin/Gentamicin	Amikacin	
q8h	1.5	5	Peak and trough with third dose
q12h	2	7	Peak and trough with third dose
q24h	2.5	9	Peak and trough with third dose
One dose	3	11	Peak and 24-hour random level; redose when random level is <2 mcg/mL (tobramycin/gentamicin) or <8 mcg/mL (amikacin)

Use actual body weight. If obese, use adjusted body weight (ABW):

- Ideal weight: Male:  $50 \text{ kg} + [2.3 \times (\text{inches} > 5 \text{ feet})]$  Female:  $45 \text{ kg} + [2.3 \times (\text{inches} > 5 \text{ feet})]$
- ABW (25% over ideal weight):  $[0.4 \times (\text{actual weight} - \text{ideal weight})] + \text{ideal weight}$
- Round dose to nearest 20 mg.

(Table continued on following page)

## TABLE 18 Traditional Aminoglycoside Dosing *(continued)*

### Serum Concentration Monitoring

- Peak serum concentrations should be drawn 30 minutes after the completion of a 30-minute infusion. Trough serum concentrations should be drawn within 30 minutes prior to the administered dose.
- Serum concentrations should be drawn around the third dose.

Desired measured serum concentrations:

	<u>Tobramycin/Gentamicin</u>	<u>Amikacin</u>	<u>Streptomycin</u>
<b>Peaks</b>			
Pneumonia	8-10 mcg/mL	28-35 mcg/mL	
Sepsis	7-10 mcg/mL	25-35 mcg/mL	
Intra-abdominal	6-8 mcg/mL	22-28 mcg/mL	
Endocarditis <sup>1</sup> /UTI	4 mcg/mL	15-20 mcg/mL	20-30 mcg/mL

Note: For synergistic effect against gram-positive organisms, peaks of 3 to 4 are sufficient (ie, gentamicin 1 mg/kg q8h; interval adjusted for renal function).

	<u>Tobramycin/Gentamicin</u>	<u>Amikacin</u>	<u>Streptomycin</u>
<b>Troughs</b>	<2 mcg/mL	<8 mcg/mL	<5 mcg/mL

For patients receiving hemodialysis:

- Administer the *same* loading dose.
- Redose *after* each dialysis if level <2 mcg/mL (tobramycin/gentamicin) or <8 mcg/mL (amikacin).
- Watch for ototoxicity from accumulation of drug.

<sup>1</sup> Gram-positive endocarditis.

## TABLE 19 Extended Interval Aminoglycoside Dosing

- Exclusion criteria for extended interval aminoglycoside dosing:
  - Age <18 years
  - Serum creatinine >1.5 or creatinine clearance <30 mL/min
  - Synergistic dosing for gram-positive infections (eg, endocarditis)
  - History of ototoxicity
  - Pregnancy
  - Cystic fibrosis patients
- Dosing regimens: dose based on actual, or if patient obese, then adjusted body weight.

<b>CrCl (mL/min)</b>	<b>Gentamicin Dose<sup>1</sup></b>	<b>Amikacin Dose<sup>2</sup></b>	<b>Interval</b>
≥60	5 mg/kg	15-18 mg/kg	q24h
30-59	5 mg/kg	15-18 mg/kg	q48h

- Dosing adjustments:

<b>Gentamicin Trough Concentration<sup>3</sup></b>	<b>Amikacin Trough Concentration<sup>3</sup></b>	<b>Dosing Recommendation</b>
<1 mcg/mL	<4 mcg/mL	Continue current dosing
1-3 mcg/mL	4-8 mcg/mL	Extend interval to 48 hours
>3 mcg/mL	>8 mcg/mL	Use traditional dosing

1 Max dose of gentamicin 500 mg.

2 Max dose of amikacin 2000 mg.

3 Serum levels should be obtained around the second dose.

## TABLE 20 Vancomycin Dosing Guidelines for Adults

1. The dose should be calculated based on patient's actual body weight:

Weight (in kg) <sup>1</sup>	Dose (in mg)
<50	750
50-74	1000
75-90	1250
>90	1500

2. The dosing interval should be based on creatinine clearance (CrCl):

CrCl Male:	$\frac{(140 - \text{age})(\text{body weight})}{72 \times \text{serum creatinine}}$
CrCl Female:	Male CrCl Value $\times$ 0.85

CrCl (mL/min)	Dosing Interval
>50	q12h <sup>2</sup>
30-50	q24h
<30	One dose, then check a random vancomycin level in 24-48 hours, redose when level is <15-20 mcg/mL
Hemodialysis	500-750 mg after each hemodialysis session

3. Vancomycin trough (pre-dose) levels should be checked:
- A. On the fifth day of therapy and weekly thereafter for most patients
  - B. Prior to the fourth dose for patients with:
    - i. Morbid obesity (BMI >40) or severe malnutrition (weight <45 kg)
    - ii. Acute renal failure (change in serum creatinine by more than 0.5 mg/dL)
    - iii. Central nervous system infections
    - iv. Endocarditis
    - v. Persistent gram-positive bacteremia

(Table continued on following page)



**TABLE 20 Vancomycin Dosing Guidelines for Adults** *(continued)*

4. Dose modifications based on the trough (pre-dose) level:

<b>Measured Trough Level (mcg/mL)<sup>3</sup></b>	<b>Dosage Adjustment</b>
<5	Half the dosage interval to next frequency AND consider increase in dose by 250-500 mg
5-10	Half the dosage interval to next frequency OR increase dose by 250-500 mg
10-15	No change if goal trough 10-20 mcg/mL. If goal trough is 15-25 mcg/mL, increase dose by 250-500 mg
15-20	No change
20-25	No change if goal trough 15-25 mcg/mL. If goal trough is 10-20 mcg/mL, decrease dose by 250-500 mg OR double the dosage interval to next frequency
>25	Double the dosage interval to next frequency AND/OR decrease the dosage

1 Morbidly obese patients may require doses >1500 mg.

2 For patients >75 years of age, it is recommended to start at a q24h interval regardless of calculated CrCl.

3 Higher trough levels (15-25) may be desirable for serious *Staphylococcus aureus* infections, such as endocarditis, device infections, high-grade bacteremia, HAP/VAP, and CNS infections.

**TABLE 21 Antimicrobial Interactions With Cyclosporine, Tacrolimus, and Sirolimus**

Antimicrobial Agent	Increase Effect		Decrease Effect		Additive Toxicity
	Cyclo/Tacro	Siro <sup>1</sup>	Cyclo/Tacro	Siro <sup>1</sup>	
Aminoglycosides					<b>XX</b> Nephrotoxicity
Amphotericin B					<b>XX</b> Nephrotoxicity
Chloroquine	<b>XX</b>				
Ciprofloxacin	X				
Clarithromycin	XX	XX			
<b>Erythromycin</b>	<b>XXX</b>	<b>XXX</b>			
Fluconazole	X	X			
Itraconazole	<b>XX</b>	<b>XX</b>			
Ketoconazole	<b>XX</b>	<b>XX</b>			
Metronidazole	X	X			
Micafungin		X			
Pyrazinamide			X		
Quinupristin/dalfopristin	XX	XX			
Rifabutin	?		X	X	
Rifampin			<b>XX</b>	<b>XX</b>	
<b>Protease Inhibitors<sup>2</sup></b>	<b>XXX</b>	<b>XXX</b>			
Trimethoprim/sulfamethoxazole			X		X Nephrotoxicity
<b>Voriconazole/posaconazole</b>	<b>XXX</b>	See footnote 3			

XXX Major interaction.

XX Moderate interaction: Significant interactions have been reported, however the incidence is either low or unknown.

X Minor interaction.

1 Limited drug interaction studies have been conducted; most data based on theoretical inhibition/induction of cytochrome 3A4.

2 Amprenavir, atazanavir, fosamprenavir, indinavir, nelfinavir, ritonavir, saquinavir, lopinavir/ritonavir, tipranavir/ritonavir.

3 Voriconazole and posaconazole are contraindicated with sirolimus.

## TABLE 22 Antimicrobial Interactions With Warfarin

Antimicrobial Agent	Increase Warfarin Effect	Decrease Warfarin Effect
Chloramphenicol	XX	
Ciprofloxacin	XX	
Delavirdine	XX	
<b>Efavirenz</b>	X	X
Erythromycin	XX	
Fluconazole	XX	
Isoniazid	X	
Itraconazole	XX	
Ketoconazole	XX	
<b>Metronidazole</b>	XXX	
Miconazole (including topical)	XX	
Neomycin (PO)	XX	
Norfloxacin	XX	
Penicillins (dicloxacillin)		XX
Rifabutin		?
<b>Rifampin</b>		XXX
<b>Protease Inhibitors</b> <sup>1,2</sup>	XXX	
Tetracyclines	X	
<b>Trimethoprim/sulfamethoxazole</b>	XXX	
Voriconazole/posaconazole	XX	

XXX Major interaction.

XX Moderate interaction: Significant interactions have been reported, however, the incidence is either low or unknown.

X Minor interaction.

1 Amprenavir, atazanavir, fosamprenavir, indinavir, nelfinavir, ritonavir, saquinavir, lopinavir/ritonavir, tipranavir/ritonavir.

2 Ritonavir may decrease warfarin effect.

## TABLE 23 Antimicrobials in Pregnancy

Antimicrobial Name (Generic)	Pregnancy Category	Antimicrobial Name (Generic)	Pregnancy Category	Antimicrobial Name (Generic)	Pregnancy Category	Antimicrobial Name (Generic)	Pregnancy Category
Abacavir	C	Ciprofloxacin	C	Fosfomycin	B	Pyrazinamide	C
Acyclovir	C	Clarithromycin	C	Ganciclovir	C	Pyrimethamine	C
Amantadine	C	Clavulanate	B	Gentamicin	C	Quinupristin/dalfopristin	B
Amikacin	D	Clindamycin	B	Indinavir	C	Raltegravir	C
Amoxicillin	B	Clofazimine	C	Isoniazid	C	Rifabutin	B
Amphotericin B	B	Colistimethate	C	Itraconazole	C	Rifampin	C
Ampicillin	B	Cytomegalovirus immune globulin	C	Ketoconazole	C	Rimantadine	C
Ampicillin/sulbactam	B	Dapsone	C	Lamivudine	C	Ritonavir	B
Amprenavir	C	Daptomycin	B	Levofloxacin	C	Saquinavir	B
Atazanavir	B	Darunavir	B	Linezolid	C	Stavudine	C
Atovaquone	C	Delavirdine	C	Lopinavir/ritonavir	C	Streptomycin	D
Atovaquone/proguanil	C	Dicloxacillin	B	Maraviroc	B	Sulfadiazine <sup>2</sup>	B
Azithromycin	B	Didanosine	B	Meropenem	B	Sulfisoxazole <sup>2</sup>	C
Aztreonam	B	Doxycycline	D	Metronidazole <sup>1</sup>	B	Tenofovir	B
Cefazolin	B	Efavirenz	D	Micafungin	C	Tetracycline	D
Cefdinir	B	Emtricitabine	B	Nelfinavir	B	Tigecycline	D
Cefixime	B	Enfuvirtide	B	Nevirapine	B	Tipranavir	C
Cefpodoxime	B	Erythromycin	B	Nitrofurantoin	B	Tobramycin	D
Cefprozil	B	Ethambutol	B	Norfloxacin	C	Trimethoprim	C
Ceftazidime	B	Etravirine	B	Oxacillin	B	TMP/SMX <sup>2</sup>	C
Ceftriaxone	B	Fluconazole	C	Oseltamivir	C	Vaccines	See note
Cefuroxime	B	Foscarnet	C	Penicillin G	B	Valganciclovir	C
Cephalexin	B	Fosamprenavir	C	Pentamidine	C	Vancomycin	C
Chloramphenicol	C			Piperacillin/tazobactam	B	Voriconazole	D
Cidofovir	C			Posaconazole	C	Zidovudine	C

1 Metronidazole is contraindicated in the first trimester.

2 Avoid near term.

**Note: Vaccines in pregnancy**—Pregnant women should receive the influenza vaccine. In addition, pregnant women should receive tetanus-diphtheria (Tdap) if not already immune. Live virus vaccines such as measles-mumps-rubella (MMR) and varicella are contraindicated in pregnancy with the exception of yellow fever vaccine. For a listing of vaccines recommended during pregnancy, refer to Table 26 (Adult Immunization).

(Table continued on following page)

## TABLE 23 Antimicrobials in Pregnancy

### *Definitions of Pregnancy Category* (continued)

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- Category A: Controlled studies in women fail to demonstrate a risk to the fetus in the first trimester, and there is no evidence of a risk in later trimesters. The possibility of fetal harm appears remote.
- Category B: Either animal-reproduction studies have not demonstrated a fetal risk, but there are no controlled studies in pregnant women; or animal-reproduction studies have shown an adverse effect (other than a decrease in fertility) that was not confirmed in controlled studies in women in the first trimester (and there is no evidence of a risk in later trimesters).
- Category C: Either studies in animals have revealed adverse effects on the fetus (embryogenic, teratogenic, or other), and there are no controlled studies in women; or studies in women and animals are not available. Drugs should be given only if the potential benefit justifies the potential risk to the fetus.
- Category D: There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (eg, the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).
- Category X: Studies in animals or human beings have demonstrated fetal abnormalities, there is evidence of fetal risk based on human experience, or both; and the risk of the use of the drug in pregnant women clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant.

## TABLE 24 Antimicrobials in Lactation

**Most antimicrobials** are **compatible** with lactation and are safe to the nursing infant with a few exceptions that are listed in the following table. It is, however, prudent to minimize maternal exposure to all medications.

### Antimicrobials Contraindicated in Lactation

Antimicrobial Name (Generic)	Notes
Chloramphenicol	Potential for idiosyncratic bone marrow suppression
Ciprofloxacin, norfloxacin (quinolones)	Ciprofloxacin is not currently approved for children. Cartilage lesions and arthropathies were seen in immature animals
Clofazimine	Clofazimine is excreted into breast milk and may result in skin pigmentation of the nursing infant
Furazolidone	Avoid in infants less than 1 month old due to potential risk of hemolytic anemia
Metronidazole	Risk of mutagenicity and carcinogenicity. American Academy of Pediatrics recommends discontinuing breast feeding for 12 to 24 hours to allow drug excretion
<b>Vaccines</b>	Vaccines are <b>compatible</b> with lactation, including live vaccines such as measles-mumps-rubella (MMR) and oral polio vaccine (OPV). There has been transfer of live vaccines to nursing infants with no ill effects noted

## TABLE 25 Community-Based Parenteral Antimicrobial Therapy (CoPAT) Guidelines

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Patients who require long-term parenteral antimicrobials may be candidates for completion of therapy at home, a subacute care unit, an extended care facility, a rehab unit or a dialysis center. All patients who may need CoPAT must be first seen and evaluated by an ID Consultation Service.

### **Process**

1. A potential need for prolonged IV antimicrobial therapy is recognized by the patient's Primary Service.
2. The Primary Service places an Infectious Disease consult (via EPIC consult request) for CoPAT and a Case Manager Consult at least 48 hours prior to the planned discharge.
3. The Infectious Disease Consultant, after evaluating the patient, confirms a need for CoPAT or suggests alternative therapy.
4. The Case Manager assesses the patient and caregiver's ability and willingness to participate in CoPAT, provides information on the availability and limitations of Home Health Care, and discusses the potential impact of home-bound status.
5. The PICC team is consulted through an order in EPIC. The PICC team is available Mon-Fri from 8 AM to 6 PM and Sat/Sun from 7 AM to 7 PM (except for Cleveland Clinic holidays) extension 45252 or pager 23520.
6. If a PICC is placed at the bedside, a standard upright chest x-ray (high-resolution technique) must be taken to verify that the tip is in the superior vena cava.
7. The Primary Service must confirm PICC tip verification, and approve use of the PICC prior to discharge.

### **Vascular Access Devices**

1. Peripherally inserted central catheters (PICCs) are flexible long line catheters used for antimicrobial infusions when therapy is planned for 2-8 weeks.
2. Midline catheters (20 cm long) are deep peripheral catheters used for short-term therapy. They are contraindicated for infusates with pH <5 or >9, such as:
  - Oxacillin
  - Penicillin
  - Amphotericin-B products
  - Erythromycin
  - Fosfarnet
  - Quinupristin/dalfopristin (Synercid)
  - Vancomycin
  - Piperacillin/tazobactam

*(Table continued on following page)*

## TABLE 25 Community-Based Parenteral Antimicrobial Therapy (CoPAT) Guidelines *(continued)*

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### **Vascular Access Devices** (continued)

3. Contraindications to placing PICCs or midline catheters include: SAME SIDE flaccid upper extremity, mastectomy, infection, DVT, A/V fistula, permanent pacemaker or implanted cardioverter device.
4. For patients who may require hemodialysis, a Hohn catheter is preferred over a PICC or midline.
5. Other tunneled venous access devices such as a Hickman catheter or subcutaneous ports may also be used for CoPAT.
6. Central venous lines that are not tunneled (ie: internal jugular, subclavian or femoral central IV catheters) are not suitable for long-term antimicrobial therapy in the home setting.

### **CoPAT Consultation Guidelines**

1. The ID resident should approach the patient like any new consult; that is, the consult should be performed “from scratch,” with a careful review of the patient’s history, hospital course, laboratory findings, radiographic studies etc.; and a complete physical examination.
2. One should not assume the patient will require CoPAT. The ID Consultant may not agree with the diagnosis, selection of antimicrobial, route of administration, length of therapy, etc.
3. If the patient needs CoPAT, vascular access must be established prior to discharge.
4. A final electronic CoPAT script must be completed by the ID Consultant prior to discharge. If the patient’s discharge is delayed more than 72 hours the script must be updated.
5. The CoPAT script provides orders for laboratory monitoring tests, lists the ID Staff physician who will be responsible for overseeing CoPAT, and specifies the date and time for an ID follow-up appointment.



## TABLE 26 Recommended Adult Immunization Schedule

Vaccine ▼ Age Group (years) ▶	19-49	50-64	≥65
Tetanus, diphtheria, pertussis (Td/Tdap)	Substitute 1 dose of Tdap for Td then 1 dose Td booster every 10 years		
Human papillomavirus	3 doses (0, 2, 6 months): females aged 19-26		Td booster q10y
Measles, mumps, rubella	1 or 2 doses	1 dose	
Varicella	2 doses (0, 4-8 weeks)		
Influenza	1 dose annually		
Pneumococcal (polysaccharide)	1-2 doses		1 dose
Hepatitis A	2 doses (0, 6-12 months or 0, 6-18 months)		
Hepatitis B	3 doses (0, 1-2, 4-6 months)		
Meningococcal	1 or more doses		
Zoster			1 dose <sup>1</sup>

↔ For all persons in this category who meet the age requirements and who lack evidence of immunity (eg, lack documentation of vaccination or have no evidence of prior infection)

↔ Recommended if some other risk factor is present (eg, on the basis of medical, occupational, lifestyle, or other indications)

<sup>1</sup> Recommended beginning at age 60. (Note: FDA approved to begin at age 50.)

(Table continued on following page)

**TABLE 26 Recommended Adult Immunization Schedule** *(continued)*

Indication ▶	Pregnancy	Immuno-compromising conditions (excluding HIV)	HIV infection: CD4 + T lymphocyte count (cells/mcL)		Diabetes, heart disease, COPD, chronic alcoholism	Asplenia (including elective splenectomy and terminal complement deficiencies)	CLD	Kidney failure, ESRD, receipt of hemodialysis	Health care personnel
			<200	≥200					
Td/Tdap	1 dose Td booster every 10 years Substitute 1 dose of Tdap for Td								
HPV	3 doses for females through 26 years of age								
MMR	Contraindicated			1 or 2 doses					
Varicella	Contraindicated			2 doses (0, 4-8 weeks)					
Influenza (annually)	1 dose TIV								1 dose TIV or LAIV
PPV	1-2 doses								
HepA	2 doses (0, 6-12 months or 0, 6-18 months)								
HepB	3 doses (0, 1-2, 4-6 months)								
Meningococcal	1 or more doses								
Zoster	Contraindicated			1 dose					

For all persons in this category who meet the age requirements and who lack evidence of immunity (eg, lack documentation of vaccination or have no evidence of prior infection)

Recommended if some other risk factor is present (eg, on the basis of medical, occupational, lifestyle, or other indications)

Adapted from: Recommended Adult Immunization Schedule. Centers for Disease Control and Prevention Web site. <http://www.cdc.gov/vaccines/recs/schedules/downloads/adult/07-08/adult-schedule.pdf>. Accessed July 7, 2010.

## TABLE 27 Isolation Precaution Quick Guide

Precautions ▶ Standard (#100) (Infection Control Policy #)	Contact (#101)	Droplet (#102)	Airborne (#103)	
Organism/ disease	Used for <b>all</b> patients regardless of diagnosis	<ul style="list-style-type: none"> <li>• <i>Burkholderia</i> sp in cystic fibrosis patient: call IC pager #21740</li> <li>• crAb in all ICUs, H63, and U31<sup>2</sup></li> <li>• KPC<sup>2</sup></li> <li>• <i>Clostridium difficile</i></li> <li>• Disseminated herpes zoster<sup>1</sup> (shingles)</li> <li>• RSV</li> <li>• SARS</li> <li>• Smallpox</li> <li>• VISA or VRSA</li> <li>• Varicella/chickenpox<sup>1</sup></li> <li>• Adenovirus<sup>3</sup></li> <li>• Parainfluenza<sup>4</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Infectious bacterial meningitis (<i>Haemophilus influenzae</i> or <i>Neisseria meningitidis</i>)</li> <li>• Influenza</li> <li>• Adenovirus<sup>3</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Disseminated herpes zoster (shingles)<sup>1</sup></li> <li>• RSV when receiving aerosolized ribavirin therapy</li> <li>• Varicella/chickenpox<sup>1</sup></li> <li>• Smallpox</li> <li>• Tuberculosis</li> </ul>
Hand hygiene	Soap and water or alcohol based hand rub	Same as <i>Standard</i> ; also <i>C difficile</i> : use soap and water	Same as <i>Standard</i>	Same as <i>Standard</i>
Signage	None	Contact Precautions <sup>5</sup>	Droplet Precautions	Airborne Precautions <sup>5</sup>
Gloves	For contact with blood and/or any body fluid	Gloves to enter room; discard upon leaving room	Same as <i>Standard</i>	Same as <i>Standard</i>

(Table continued on following page)

**TABLE 27 Isolation Precaution Quick Guide** *(continued)*

<b>Precautions ▶ Standard (#100) (Infection Control Policy #)</b>	<b>Contact (#101)</b>	<b>Droplet (#102)</b>	<b>Airborne (#103)</b>	
Gown	To protect clothing when splash and/or spray likely	Gown to enter room; discard upon leaving room	Same as <i>Standard</i>	TB: Same as <i>Standard</i> Varicella/disseminated zoster; gown and glove for contact with lesions
Mask/eye protection	Wear to protect eyes, nose, and mouth when splash and/or spray likely	Same as <i>Standard</i> <sup>6</sup>	Surgical mask	Respirator <sup>7</sup>
Patient placement	No restrictions	Private room; may cohort patients	Same as <i>Contact</i> ; plus keep door closed	Private NEGATIVE AIR PRESSURE ROOM; keep door closed
Patient-care equipment	Clean and disinfect equipment after use; limit patient supplies in rooms	Use designated equipment whenever possible (ie, dedicated BP cuff and stethoscope)	Same as <i>Standard</i>	Same as <i>Standard</i>
Patient transport	No restrictions	Cover wheelchair/cart; have patient clean hands and don clean gown before ambulation <sup>8</sup>	Surgical mask on patient <sup>8</sup>	Surgical mask on patient <sup>8</sup>

1 Chickenpox and disseminated zoster: use *Contact AND Airborne Precautions*.

2 History of or positive culture in any site.

3 For BMT/heme-onc/solid organ transplant only. Use contact and airborne precautions.

4 For BMT/heme-onc/solid organ transplant only.

5 EXCEPTION: Use chickenpox sign for varicella and disseminated herpes zoster.

6 RSV: NEGATIVE AIR with N-95 or PAPR only if receiving ribavarin.

7 EXCEPTION: Respirator not needed for varicella or disseminated herpes zoster (ONLY IMMUNE EMPLOYEES TO ENTER).

8 Include in Hand Off communication.

## TABLE 28 Guidelines for Antimicrobial Prophylaxis for Clean and Clean-Contaminated Surgical Wounds

*All Preoperative Doses Must Be Given Within 1 Hour<sup>1</sup> Prior to Surgical Incision<sup>2</sup>*

Nature of Operation	Antimicrobial <sup>3</sup> Program	Penicillin-Allergic Patient
Cardiothoracic	Routine prophylaxis: Cefuroxime 1.5 g q12h MRSA colonized patients: Cefuroxime 1.5 g q12h PLUS vancomycin 1 g q12h	With or without MRSA colonization, aortic graph material installed, LVAD: Vancomycin 1 g q12h PLUS ciprofloxacin 400 mg q12h
Colorectal	Ampicillin/sulbactam 3 g	Ciprofloxacin 400 mg AND metronidazole 500 mg OR Ciprofloxacin 400 mg AND clindamycin 900 mg
General surgery	Cefazolin 1 g	Vancomycin 1 g OR clindamycin 900 mg
Neurosurgical	Cefazolin 1 g	Vancomycin 1 g
Orthopedics	Cefazolin 1 g <sup>4</sup>	Vancomycin 1 g OR clindamycin 900 mg
Vascular Surgery	Cefazolin 1 g <sup>4</sup> OR cefuroxime 1.5 g	Vancomycin 1 g OR clindamycin 900 mg

1 Vancomycin should be given within 2 hours prior to surgical incision.

2 If duration of surgical procedure is >4 hours, patient should receive a second prophylactic dose intraoperatively.

3 Total duration must be 24 hours for noncardiothoracic surgery and 48 hours for cardiothoracic surgery.

4 Consider 2 g in patients >100 kg.

## TABLE 29 Guidelines for Prophylaxis of Infective Endocarditis

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### Highest Risk Patients for Adverse Outcomes From Endocarditis

- Prosthetic cardiac valve disease
- Previous infective endocarditis
- Congenital heart disease (CHD):
  - Unrepaired cyanotic
  - Completely repaired with prosthetic materials for 6 months after procedure, allowing for endothelial formation
  - Incompletely repaired with residual defects at prosthetic patches or devices
- Cardiac transplantation with valvular defects

### Invasive Procedures for Prophylaxis in High-Risk Patients

- Any procedure that involves the gingival tissues or periapical region of a tooth and for those procedures that perforate the oral mucosa
- Cystoscopy or other genitourinary tract manipulation when the urinary tract is infected with *Enterococcus* species
- Drainage of established infections, such as empyema, abscesses, or phlegmons where *Staphylococcus aureus*, streptococci, or enterococci are likely or proven pathogens

(Table continued on following page)

**TABLE 29 Guidelines for Prophylaxis of Infective Endocarditis** *(continued)*

**Antimicrobials for Infective Endocarditis Prophylaxis (AHA 2007)**

**Invasive Procedures for Prophylaxis in High-Risk Patients**

<b>Situation</b>	<b>Agent</b>	<b>Regimen (30-60 minutes before procedure)</b>
Oral	Amoxicillin	2 g
Penicillin-allergic	Cephalexin <sup>1</sup> or Clindamycin or Azithromycin	2 g 600 mg 500 mg
Unable to take oral	Ampicillin or Cefazolin or ceftriaxone <sup>1</sup>	2 g IM/IV 1 g IM/IV
Penicillin-allergic	Cefazolin or ceftriaxone <sup>1</sup> Clindamycin	1 g IM/IV 600 IM/IV

<sup>1</sup> Cephalosporins should not be used in an individual with a history of anaphylaxis, angioedema, or urticaria with penicillins or ampicillin.

**TABLE 30 Solid-Organ Transplant:  
Antimicrobial Prophylaxis<sup>1</sup>**

<b>Infection</b>	<b>Preferred Regimen</b>	<b>Alternatives</b>
<b>Kidney/Pancreas</b>		
PCP and UTI	TMP/SMX SS (80/400) PO q24h for life of allograft	Aerosolized Pentamidine 300 mg once monthly × 1 year
Fungal	Clotrimazole troche 10 mg PO tid × 1 month. If ureteral stent, then fluconazole 100 mg PO q24h until stent removed (usually 6 to 8 wk)	
<b>Heart</b>		
PCP	TMP/SMX DS (160/800) PO MWF × 1 year	Aerosolized Pentamidine 300 mg once monthly × 1 year; Dapsone 100 mg PO q24h × 1 year
Fungal	Clotrimazole troche 10 mg PO qid × 1 month, <i>OR</i> Nystatin 5 mL (500,000 units) PO qid swish and swallow × 1 month	
<b>Liver</b>		
PCP	TMP/SMX DS (160/800) PO MWF for life	Aerosolized Pentamidine 300 mg once monthly or dapsone 100 mg PO q24h
Fungal	Clotrimazole troche 10 mg qid × 1 month	Nystatin 5 mL PO swish and swallow qid × 1 month
<b>Lung</b>		
PCP	TMP/SMX DS (160/800) PO MWF for life	Dapsone 100 mg PO MWF, <i>OR</i> aerosolized Pentamidine 300 mg once monthly if G6PD deficient
Fungal	Amphotericin B 10 mg inhaled q12h until therapeutic itraconazole level <sup>2</sup> then Itraconazole 200 mg PO q24h × 18 months	

*(Table continued on following page)*



**TABLE 30 Solid-Organ Transplant:  
Antimicrobial Prophylaxis<sup>1</sup> (continued)**

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**Small Bowel**

PCP	TMP/SMX 160 mg IV PO MWF; when taking PO change to TMP/SMX DS (160/800) MWF for life	Aerosolized pentamidine 300 mg once monthly for life
Fungal	Micafungin 100 mg IV q24h × 1 month	

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1 Guidelines subject to change; please check website version for most current recommendations.

2 Trough level >250 mcg/mL; usually achieved around day 10 to 14.

# TABLE 31 Solid-Organ Transplant: CMV Prophylaxis<sup>1</sup>

CMV Status	Regimen
<b>Heart</b>	
D-/R-	Acyclovir <sup>3</sup> 200 mg PO TID × 1 month
D-/R+ <sup>2</sup>	Valganciclovir <sup>3</sup> 900 mg PO q12h × 2 wk, then valganciclovir <sup>3</sup> 900 mg PO q24h × 2 wk, then acyclovir <sup>3</sup> 800 mg PO qid for months 2 and 3
D+/R+ <sup>2</sup>	Same as D-/R+
D+/R- <sup>2</sup>	Same as D-/R+
<b>Lung<sup>4</sup></b>	
D-/R- <sup>5</sup>	Ganciclovir <sup>3</sup> 5 mg/kg IV q12h until able to take oral, then acyclovir <sup>3</sup> 400 mg PO tid × 180 days
D-/R+ <sup>5</sup>	Ganciclovir <sup>3</sup> 5 mg/kg IV q12h until able to take oral, then valganciclovir <sup>3</sup> 900 mg PO q24h × 1 year
D+/R+ <sup>5</sup>	Same as D-/R+
D+/R- <sup>5</sup>	Same as D-/R+
<b>Kidney</b>	
D-/R-	Acyclovir <sup>3</sup> 200 mg PO tid × 3 months
D-/R+	Valganciclovir <sup>3</sup> 900 mg PO q24h × 3 months
D+/R+	Valganciclovir <sup>3</sup> 900 mg PO q24h × 3 months
D+/R-	Valganciclovir <sup>3</sup> 900 mg PO q24h × 3 months (× 6 months for pancreas and kidney pancreas)

1 Guidelines subject to change; please check website for most current recommendations.

2 Patients unable to tolerate oral medications by day 7, ganciclovir<sup>4</sup> 5 mg/kg IV q12h × 2 wk then 6 mg/kg IV q24h × 2 wk; change to valganciclovir when able to tolerate oral medications.

3 **Renal dosage adjustment necessary.**

4 CMV DNA checked at least every 2 weeks for first year.

5 If patients unable to tolerate oral medications by day 14, decrease to ganciclovir 2.5 mg/kg IV q12h.

(Table continued on following page)

**TABLE 31 Solid-Organ Transplant: CMV Prophylaxis<sup>1</sup>** *(continued)*

CMV Status	Regimen	
<b>Liver</b>		
D-/R-	Acyclovir 400 mg PO bid × 3 months	
D-/R+	Ganciclovir <sup>2</sup> 5 mg/kg IV q12h × 14 d (may change to valganciclovir <sup>2</sup> 900 mg PO bid if patient discharged within 14 days of transplant) then acyclovir 400 mg PO bid × 3 months	
D+/R+	Same as D-/R+	
D+/R-	Same as D-/R+	
<b>Small Bowel</b>		
D-/R-	Ganciclovir <sup>2</sup> 5 mg/kg IV q12h until able to take oral, then valganciclovir <sup>2</sup> 450 mg PO bid × 6 months	
D-/R+	Same as D-/R-	
D+/R+	Same as D-/R-	
D+/R-	Same as D-/R- PLUS CMV immune globulin 50 mg/kg once monthly × 6 months	
<b>Valganciclovir<sup>4</sup></b>		
CrCl (mL/min)	Induction <sup>3</sup>	Maintenance <sup>5</sup>
≥60	900 mg bid	900 mg q24h
40-59	450 mg bid	450 mg q24h
25-39	450 mg q24h	450 mg q2d
10-24	450 mg q2d	450 mg twice weekly
<b>Ganciclovir IV</b>		
CrCl (mL/min)	Dose	
>80	5 mg/kg q12h	
50-79	2.5 mg/kg q12h	
25-49	2.5 mg/kg q24h	
<25	1.25 mg/kg q24h	
<b>Acyclovir</b>		
CrCl (mL/min)	Dose	
>50	q6-8h	
25-50	q8-12h	
<25	q12h	

1 Guidelines subject to change; please check website for most current recommendations.

2 **Renal dosage adjustment necessary.**

3 Heart and liver transplants use 2 wk of induction followed by maintenance dosing or a change to acyclovir.

4 Monitor CBC; valganciclovir may cause bone marrow suppression.

5 Lung and kidney transplants ONLY use maintenance dosing.

**TABLE 32 Bone Marrow Transplant:  
Antimicrobial and CMV Prophylaxis**

<b>Infection</b>	<b>Regimen</b>
<b>Autologous Stem-Cell Transplants</b>	
Bacterial	Ciprofloxacin <sup>1</sup> 500 mg PO bid starting at admission <sup>2</sup>
Viral	Acyclovir 250 mg IV q12h or 400 mg PO bid
<b>Allogeneic Stem-Cell Transplants</b>	
Bacterial	TMP/SMX DS q12h starting at admission <sup>2</sup>
Fungal:	
Pre-engraftment	Amphotericin B 0.2 mg/kg/d starting day +1 <sup>3</sup>
Post-engraftment	Itraconazole solution 200 mg PO q24h <sup>4</sup>
Viral:	
Patients will have weekly CMV PCR for the first 3 months after transplant, then every 2 weeks for 3 months if tests are negative.	
Monitoring should continue for patients treated with immunosuppressive therapy for GVHD due to the risk of CMV reactivation.	
Asymptomatic patient with viral load >1,000 copies/mL: valganciclovir <sup>1</sup> 900 mg PO bid	
Symptomatic patient or viral load >10,000 copies/mL: ganciclovir <sup>1</sup> 5 mg/kg IV q12h	

1 Renal dose adjustment necessary.

2 If fever develops, discontinue and begin broad spectrum antimicrobials (see Table 12).

3 Change to voriconazole if concern for infection.

4 For patients unable to tolerate itraconazole, posaconazole suspension 200 mg PO tid with high-fat meal or nutritional supplement.

**TABLE 33 Antimicrobial Cost Data for the Cleveland Clinic**

<b>Drug</b>	<b>Dose</b>	<b>Doses/d</b>	<b>Cost/d<sup>1</sup></b>	<b>Cost/wk<sup>2</sup></b>
Acyclovir	500 mg q8h	3	\$25	\$180
Amikacin	500 mg q12h	2	\$5	\$35
Amphotericin B	50 mg q24h	1	\$5	\$40
Amphotericin B Lipid Complex	3 mg/kg q24h	1	\$150	\$1050
Ampicillin	1 g q6h	4	\$10	\$60
Ampicillin/sulbactam	3 g q8h	3	\$30	\$220
Azithromycin	500 mg q24h	1	\$10	\$70
Azithromycin (PO)	500 mg q24h	1	\$5	\$30
Aztreonam	1 g q8h	3	\$100	\$700
Cefazolin	1 g q8h	3	\$10	\$80
Ceftazidime	1 g q8h	3	\$20	\$140
Ceftriaxone	1 g q24h	1	\$10	\$70
Ceftriaxone	2 g q24h	1	\$20	\$140
Cefuroxime	750 mg q8h	3	\$15	\$120
Cefuroxime	1.5 g q8h	3	\$30	\$200
Cidofovir	5 mg/kg OW×2 wk	N/A	N/A	\$700
Ciprofloxacin	400 mg q12h	2	\$5	\$35
Ciprofloxacin (PO)	750 mg bid	2	\$0.25	\$2.00
Clindamycin	600 mg q8h	3	\$10	\$80
Daptomycin	500 mg q24h	1	\$240	\$1700
Ertapenem	1 g q24h	1	\$50	\$350
Erythromycin	1 g q6h	4	\$10	\$80
Fluconazole	200 mg q24h	1	\$10	\$70
Fluconazole	400 mg q24h	1	\$15	\$105
Fluconazole (PO)	200 mg q24h	1	\$0.40	\$3
Foscarnet	6.3 g q12h	2	\$105	\$720
Fosfomycin (PO)	3 g single dose	1	\$30	Not applicable

*(Table continued on following page)*

**TABLE 33 Antimicrobial Cost Data for the Cleveland Clinic** *(continued)*

<b>Drug</b>	<b>Dose</b>	<b>Doses/d</b>	<b>Cost/d<sup>1</sup></b>	<b>Cost/wk<sup>2</sup></b>
Ganciclovir	350 mg q12h	2	\$45	\$300
Ganciclovir (PO)	1 g q8h	3	\$45	\$300
Gentamicin	80 mg q8h	3	\$5	\$20
Linezolid (IV)	600 mg q12h	2	\$190	\$1340
Linezolid (PO)	600 mg q12h	2	\$150	\$1050
Meropenem (IV)	500 mg q6h	4	\$40	\$280
Metronidazole	500 mg q6h	4	\$10	\$60
Micafungin	150 mg q24h	1	\$120	\$840
Oxacillin	2 g q4h	6	\$25	\$160
Piperacillin/tazobactam	3.375 mg q6h	4	\$60	\$420
Posaconazole (PO)	200 mg q8h	3	\$90	\$620
Tigecycline (IV)	50 mg q12h	2	\$120	\$840
Tobramycin	80 mg q8h	3	\$10	\$80
TMP/SMX	320 mg q6h <sup>3</sup>	4	\$10	\$80
TMP/SMX (PO)	160 mg q12h	2	\$5	\$20
Valganciclovir (PO)	900 mg q12h	2	\$100	\$700
Vancomycin	1 g q12h	2	\$10	\$70
Vancomycin (PO)	125 mg q6h	4	\$40	\$280
Voriconazole (IV)	200 mg q12h	2	\$215	\$1500
Voriconazole (PO)	200 mg q12h	2	\$80	\$560

1 Rounded to nearest \$5.00.

2 Rounded to nearest \$20.00.

3 Based on trimethoprim.

**Note:** All agents are IV unless otherwise specified. **All costs include the piggy-back containers.** Nursing administration and pharmacy preparation time are not included.

## TABLE 34 Guidelines for Selected Antimicrobial Dosing in Adults Receiving Continuous Venovenous Hemodialysis

- Many factors affect drug clearance during continuous venovenous hemodialysis (CVVHD), including:
  - Drug molecular weight
  - Lipophilicity
  - Protein binding and volume of distribution
  - Dialysis filter porosity and surface area
  - Blood flow rate through dialysis filter
  - Others.
- Doses listed are based on clinical studies of CVVHD drug clearance when available. Otherwise, dosage recommendations are based on the drug's:
  - Pharmacokinetics
  - Estimated GFR provided by CVVHD
  - Extent of removal by IHD, if known.
- Factors that should also be considered when selecting antimicrobial doses include:
  - Site and severity of infection
  - Clinical response.

Antimicrobial	Recommended CVVHD Dose
Acyclovir	5-10 mg/kg q12-24h
Amikacin	15-20 mg/kg × 1 (adjust based on goal peak and troughs)
Ampicillin	1-2 g q6-8h
Ampicillin/sulbactam	3 g q6-8h
Azithromycin	250-500 mg q24h
Aztreonam	1 g q8h
Cefazolin	1-2 g q8h
Ceftazidime	1-2 g q8-12h

(Table continued on following page)

**TABLE 34 Guidelines for Selected Antimicrobial Dosing in Adults Receiving CVVHD** *(continued)*

<b>Antimicrobial</b>	<b>Recommended CVVHD Dose</b>
Ceftriaxone	1 g q24h (2 g q12h for meningitis, 2 g q24h for endocarditis)
Ciprofloxacin	400 mg q12h
Clindamycin	600-900 mg q8h
Colistin	1-1.5 mg/kg q8h
Daptomycin	6 mg/kg q24h
Doxycycline	100 mg q12h
Fluconazole	400-800 mg q24h
Ganciclovir	Induction: 2.5 mg/kg q12h; Maintenance: 2.5 mg/kg q24h
Gentamicin	5-6 mg/kg × 1 (adjust based on goal peak and troughs)
Linezolid	600 mg q12h
Meropenem	500 mg q8h or 1 g q12h
Metronidazole	500 mg q8h
Micafungin	100 mg q24h
Moxifloxacin	400 mg q24h
Oxacillin	2 g q4-6h
Penicillin G	2-4 million units q4-6h
Piperacillin/tazobactam	3.375 g q6-8h
Tigecycline	100 mg × 1, 50 mg q12h
Tobramycin	5-6 mg/kg × 1 (adjust based on goal peak and troughs)
TMP/SMX	5 mg/kg TMP component q12h
Vancomycin	15 mg/kg q24h (adjust based on troughs)
Voriconazole	400 mg q12h × 2, 200 mg q12h



**TABLE 35 Percentage of Bacteria Susceptible to Various Antimicrobial Agents at the Cleveland Clinic<sup>1</sup>**

Organism	Antimicrobial								
	Gent	Amp	Amp/Sulb	Cefazolin <sup>2</sup>	Cftx	Pip/Tazo	TMP/SMX	Cipro	Mero <sup>1</sup>
<i>Acinetobacter baumannii</i>	21	0	27	0	0	13	14	11	20
<i>Citrobacter freundii</i>	95	0	0	0	69	69	69	88	100
<i>Citrobacter koseri</i>	97	0	—	—	100	94	94	97	100
<i>Enterobacter aerogenes</i>	98	0	0	0	81	80	100	98	98
<i>Enterobacter cloacae</i>	91	0	0	0	70	74	83	87	100
<i>Escherichia coli</i>	91	46	58	88	96	92	72	67	100
<i>Klebsiella pneumoniae</i>	87	0	69	86	79	77	77	76	90
<i>Proteus mirabilis</i>	96	86	94	93	99	99	82	78	92

Organism	Antimicrobial							
	Gent	Tobra	Amik	Ceftaz	Pip/Tazo	TMP/SMX	Cipro	Mero <sup>1</sup>
<i>Pseudomonas aeruginosa</i>	73	85	93	79	82	0	68	76
<i>Stenotrophomonas (Xanthomonas) maltophilia</i>	—	—	—	48	—	91	—	0

1 In 2010, imipenem was tested. Imipenem susceptibilities correlate with meropenem susceptibilities.

2 Susceptibilities reported are from 2009.

(Table continued on following page)

**TABLE 35 Percentage of Bacteria Susceptible to Various Antimicrobial Agents at the Cleveland Clinic<sup>1</sup> (continued)**

Organism	Antimicrobial									
	Pcn	Cftx	Amp	Vanc	Clinda	TMP/SMX	Tetracycline	Erythro	Lin	Dapto
<i>Staphylococcus aureus</i> <sup>2</sup>										
MSSA	20	—	—	100	95	98	95	63	N/A <sup>3</sup>	N/A <sup>3</sup>
MRSA	0	0	0	100	63	91	88	0	100	91
Coagulase-negative staphylococci	9	N/A	N/A	100	N/A	67	88	36	N/A	N/A
<i>Enterococcus</i> <sup>4</sup>										
VSE	86	N/A	91	100	N/A	N/A	26	N/A	N/A	N/A
VRE <sup>5</sup>	0	0	0	0	N/A	N/A	10	N/A	100	96
<i>Streptococcus pneumoniae</i> <sup>6</sup>	89	93	—	100	61	53	64	37	N/A	N/A

1 Results are from species represented by at least 10 isolates tested between 1/1/10 and 12/31/10 from **Cleveland Clinic inpatients**.

2 Oxacillin-susceptible staphylococci are also susceptible to cefazolin, ampicillin/sulbactam, and piperacillin/tazobactam. **MRSA makes up 50% of the total *S aureus* isolates.**

3 N/A = data not applicable to that isolate or not available.

4 High-level aminoglycoside resistance in vancomycin-resistant enterococcus (VRE) = 69% for gentamicin and 64% for streptomycin; for vancomycin-susceptible enterococcus (VSE), 15% for gentamicin and 17% for streptomycin.

5 VRE makes up 25% of total *Enterococcus* isolates.

6 11% of *S pneumoniae* were intermediate in their MIC to penicillin and 0% were fully resistant.

# Glossary of Abbreviations / Acronyms

AIDS	acquired immune deficiency syndrome	CPIS	clinical pulmonary infection score	GVHD	graft-vs-host disease
Amp	ampicillin	crAb	carbapenem-resistant <i>Acinetobacter baumannii</i>	h	hour(s)
Amp/Sulb	ampicillin/sulbactam	CrCl	creatinine clearance	H/D	hemodialysis
ANC	absolute neutrophil count	CVVHD	continuous venovenous hemodialysis	HACEK	<i>Hemophilus, Actinobacillus, [group] Cardiobacterium, Eikinella, Kingella</i>
ARDS	acute respiratory distress syndrome	Cyclo	cyclosporine	HAP	hospital-acquired pneumonia
ARV	antiretroviral	d	day(s)	HBIG	hepatitis B immune globulin
bid	twice a day	D	donor	heme-onc	hematology-oncology
BMT	bone marrow transplant	D +/-	seropositive/seronegative D	HepA	hepatitis A vaccine
BP	blood pressure	Dapto	daptomycin	HepB	hepatitis B vaccine
CAD	cryptococcal antigen detection	DRV	darunavir	Hib	Haemophilus influenzae type B [vaccine]
Cap	capsule	DS	double strength	HIV	human immunodeficiency virus
CAP	community-acquired pneumonia	DT	diphtheria-tetanus [toxoid]	HPV	human papilloma virus
CBC	complete blood cell count	EFV	efavirenz	HR	heart rate
CDAD	<i>Clostridium difficile</i> -associated diarrhea	EIAD	extended interval aminoglycoside dosing	HSV	herpes simplex virus
CDC	Centers for Disease Control and Prevention	Erythro	erythromycin	ICU	intensive-care unit
Ceftaz	ceftazidime	ESRD	end-stage renal disease	ID	infectious disease
Cftx	ceftizoxime	ETR	etravirine	IE	infective endocarditis
Chloramph	chloramphenicol	FQ	fluoroquinolone	IgE	immunoglobulin E
Cipro	cirpofloxacin	FiO <sub>2</sub>	fractional concentration of oxygen in inspired gas	IgG	immunoglobulin G
CLD	chronic liver disease	g	gram	IHD	intermittent hemodialysis
Clinda	clindamycin	Gent	gentamicin	IM	intramuscular
CMV	cytomegalovirus	GFR	glomerular filtration rate	Inj	injection
CNS	central nervous system	GI	gastrointestinal	IP	intraoperative
CNS	coagulase-negative staphylococci	GNB	gram-negative bacilli	IPV	inactivated poliomyelitis vaccine
CoPAT	community-based parenteral antimicrobial therapy	GNC	gram-negative cocci	IV	intravenous
		GPB	gram-positive bacilli	IVIG	intravenous immunoglobulin
		G6PD	glucose-6-phosphate dehydrogenase	kg	kilogram
		GPC	gram-positive cocci	KPC	carbapenem-resistant

## Glossary of Abbreviations/ Acronyms *(continued)*

	<i>Klebsiella pneumoniae</i>	OD	once a day	SARS	severe acute respiratory syndrome
LAIV	live-attenuated influenza virus vaccine	OPV	oral polio vaccine	SC	subcutaneous
LD	loading dose	OW	once weekly	Siro	sirolimus
Lin	linezolid	PABA	para-aminobenzoic acid	Sol	solution
LVAD	left ventricular assist device	PaO <sub>2</sub>	partial pressure of oxygen in arterial blood	STAT	at once
MBAL	mini bronchial alveolar lavage	PAPR	powered air purifying respirator	Susp	suspension
mcg	microgram	Pcn	penicillin	Tab	tablet
MD	maintenance dose	PCP	<i>Pneumocystis carinii</i> pneumonia	Tacro	tacrolimus
MDR	multi-drug resistant	PCR	polymerase chain reaction	Td	tetanus-diphtheria [vaccine]
mg	milligram	P/D	peritoneal dialysis	Tdap	tetanus-diphtheria-pertussis [vaccine]
MIC	minimal inhibitory concentration	PI	protease inhibitor	TDF	tenofovir
min	minute(s)	PICC	peripherally inserted central catheters	tid	three times a day
mL	milliliter	PID	pelvic inflammatory disease	TIG	tetanus immunoglobulin
MMR	measles-mumps-rubella [vaccine]	Pip	piperacillin	TIV	trivalent inactivated influenza virus vaccine
MRSA	methicillin-resistant <i>Staphylococcus aureus</i>	Pip/Tazo	piperacillin/tazobactam	TMP/SMX	trimethoprim/sulfamethoxazole
MSM	men who have sex with men	PO	oral	UTI	urinary tract infection
MSSA	methicillin-sensitive <i>Staphylococcus aureus</i>	Powd	powder	Vanc	vancomycin
MSSE	methicillin-sensitive <i>Staphylococcus epidermidis</i>	PPV	pneumococcal polysaccharide vaccine	VAP	ventilator-associated pneumonia
MVP	mitral valve prolapse	PR	by way of the rectum	VISA	vancomycin-intermediate <i>Staphylococcus aureus</i>
MWF	Monday-Wednesday-Friday	PVE	prosthetic valve endocarditis	VRE	vancomycin-resistant enterococcus
NA	not applicable	q	every	VRSA	vancomycin-resistant <i>Staphylococcus aureus</i>
ND	no data	qid	four times a day	VSE	vancomycin-susceptible enterococcus
NG	nasogastric	R	recipient	VZV	varicella-zoster virus
NPO	nothing by mouth	R+/-	seropositive/seronegative R	WBC	white blood cell [count]
NVP	nevirapine	RIG	rabies immune globulin	wk	week(s)
		RR	respiratory rate		
		RSV	respiratory syncytial virus		
		RTV	ritonavir		

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