Antibiotics

Ampicillin/Sulbactam

Ampicillin/sulbactam is a beta-lactam/beta lactamase inhibitor combination antibiotic. It has activity against MSSA, streptococci, enterococci, and anaerobes. It also has activity against enteric Gram-negative organisms. However, an increasing number of *E. coli* and *Proteus* spp. are now resistant. Because of this, its use for empiric treatment of intraabdominal infections is no longer advised unless pathogen susceptibilities are known.

Acceptable uses

- Treatment of human or animal bites if parenteral therapy is needed.
- Treatment of oral infections
- Treatment of lung abscess
- Treatment of culture-negative endocarditis (ID consult advised)
- Treatment of multi-drug resistant (MDR) *Acinetobacter* spp. (ID consult advised)
- Treatment of uncomplicated vancomycin-resistant enterococcal UTIs (ampicillin can be used without sulbactam in this case)

Unacceptable uses

- Empiric treatment of biliary tract infections, diverticulitis, or secondary/peritonitis/GI perforation. Use should be limited to infections that are proven to be susceptible.

Dose

1.5-3 g IV q6-8h (higher doses may be used for infections due to MDR *Acinetobacter* spp.)

Ceftaroline

ID consult or ASP approval is <u>required</u>

Ceftaroline is a new broad-spectrum cephalosporin with a spectrum of activity similar to ceftriaxone, but with activity against MRSA. Ceftaroline demonstrates *in vitro* activity against resistant Gram-positive pathogens including methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus faecalis* (not *E. faecium*) as well as common Gram-negative pathogens such as *Haemophilus influenzae* and enteric Gram-negative bacilli, such as *Escherichia coli* and *Klebsiella pneumoniae*. Ceftaroline does not have activity against extended-spectrum beta-lactamase producing or AmpC-derepressed Enterobacteriaceae or most nonfermentative Gram-negative bacilli, such as *Pseudomonas* and *Acinetobacter*. Ceftaroline demonstrates limited activity against anaerobes such as *Bacteroides fragilis*.

Ceftaroline is FDA-approved for treatment of skin/skin structure infections (including cases caused by MRSA) and community-acquired pneumonia (including cases caused by penicillin-resistant *S. pneumoniae*). While there are animal models and case reports of successful use of ceftaroline for the treatment of osteomyelitis, bacteremia, and endocarditis, ceftaroline is not yet FDA-approved for these indications.

Acceptable uses

- Complicated skin/skin structure infections*
- Community-acquired bacterial pneumonia*
- Salvage for sustained MRSA bacteremia/endocarditis*

*All must meet the following criteria for use:

- Where MRSA is highly suspected or documented AND vancomycin is not an option
- MRSA with a vancomycin MIC ≥ 2
- Sustained difficulty in achieving appropriate vancomycin levels despite clinical pharmacy assistance with pharmacokinetics or where a vancomycin continuous infusion is not an option.
- Treatment of mixed infections, requires documentation of susceptibility

Unacceptable uses

- Selected over vancomycin in patients with renal failure solely as a reason to avoid vancomycin
- Selected solely for convenience

Dose

- 600 mg IV q12h
- MRSA bloodstream infections/endocarditis may require higher dosing and should only be undertaken with Infectious Diseases or Antimicrobial Stewardship Program input.

Toxicity

- Similar to other cephalosporins, generally well-tolerated.

Ceftazidime-Avibactam

ID consult or ASP approval is required

Ceftazidime/avibactam is a combination antimicrobial consisting of cephalosporin and novel beta-lactamase inhibitor. The pharmacology and pharmacokinetics of ceftazidime is well-established as an inhibitor of the penicillin-binding proteins of gram-negative organisms (including P. aeruginosa) resulting in the inhibition of cell-wall biosynthesis.

Avibactam is a novel non-beta-lactam beta-lactamase inhibitor with activity against Ambler class A (ESBL and KPC enzymes) and Ambler class C (AmpC enzymes) beta-lactamases and some Ambler Class D enzymes. By itself, avibactam has minimal intrinsic antimicrobial activity.

Based upon the critical need to protect the utility of novel anti-infectives, ceftazidime/avibactam should be reserved for those patients with little or no other treatment alternatives. Ceftazidime/avibactam will be reserved primarily for the management of infections caused by carbapenem-resistant Enterobacteriaceae (CRE). Of note: ceftazidime/avibactam 2.5 gram vial consists of ceftazidime 2 g plus avibactam 0.5 g. Doses are infused over 2 hours

Acceptable uses:

- In patients with a DOCUMENTED multi-drug resistant (MDR) or CRE organisms as a primary source of infection.
- In patients with a RECENT history of an MDR/CRE infection. MDR/CRE infection will need to be documented for continued use beyond 72 hours.

Unacceptable uses:

- Empiric use in patients without a DOCUMENTED infection or recent history of an MDR/CRE organism(s).
- Use in patients where alternative agents may be used.

Ceftolozane/ tazobactam

ID consult or ASP approval is <u>required</u>

Ceftolozane is a novel cephalosporin combined with a well-established beta-lactamase inhibitor, tazobactam, demonstrating in vitro activity against the more common extended-spectrum-beta-lactamase (ESBL)-producing Enterobacteriaceae and multi-drug-resistant P. aeruginosa. It is structurally similar to ceftazidime with a modified side chain. This structural change confers potent activity verses P. aeruginosa (including carbapenem-resistant P. aeruginosa) while evading the multiple mechanisms of resistance that P. aeruginosa may employ; it has no activity against carbapenem-resistant Enterobacteriaceae (CRE).

Based upon the critical need to protect the utility of novel anti-infectives, ceftolozane/tazobactam should be reserved for those patients with little or no other treatment alternatives.

Acceptable uses:

- In patients with a DOCUMENTED multi-drug resistant (MDR) organism as a primary source of infection.
- In patients with a RECENT history of an infection caused by a MDR organism. Infection caused by a MDR organism, will need to be documented for continued use beyond 72 hours.

Unacceptable uses:

- Empiric use in patients without a DOCUMENTED infection or recent history of an MDR organism
- Use in patients where alternative agents may be used

Cidofovir

ID consult or ASP approval is <u>required</u>

Cidofovir is a nucleotide analogue most commonly employed to treat cytomegalovirus (CMV) retinitis in AIDS patients. It demonstrates activity against many DNA viruses, including herpesviruses and UL97 phosphotransferase-negative CMV, which is resistant to ganciclovir. However, clinical efficacy has been demonstrated only against CMV. Cidofovir causes dose-dependent nephrotoxicity (50%) and a Fanconi-type syndrome (including proteinuria, glucosuria, and bicarbonate wasting), which can be reduced by co-administration with saline and probenecid. The drug is contraindicated in patients with serum creatinine greater than 1.5 mg/dL. Serum creatinine and urine protein should be monitored closely and dose reduction or discontinuation is required if patients develop renal dysfunction.

At UCLA Health, use of cidofovir requires Infectious Diseases consultation for use. If administered, patients should receive one liter of normal saline immediately preceding dosing and following administration. Patients should also receive probenecid (2 g PO 3 hours prior and 1 g 2 and 8 hours following cidofovir). Cidofovir should be avoided whenever possible unless other antivirals (such as ganciclovir and foscarnet) cannot be used.

Acceptable Uses:

- CMV retinitis in AIDS patients, when administered by Ophthalmology
- Treatment of select viral infections, such as adenovirus, under Infectious Diseases guidance and recommendation.

Unacceptable uses:

- Routine treatment of viral infections when other less toxic drugs (acyclovir, ganciclovir, foscarnet) are available

Colistin

ID consultation or ASP approval is <u>required</u>

Colistin is a polymyxin antibiotic. It has activity against most Gram-negative bacilli, including many multi-drug resistant *Enterobactericiae, Acinetobacter* spp. *and P. aeruginosa*. Notably, it is not active against the following Gram-negative genera: *Proteus, Serratia, Providencia, Burkholderia*, as well as Gram-negative cocci, Gram-positive organisms, or anaerobes.

Acceptable uses

- Management of infections due to multi-drug resistant *Enterobactericiae, Acinetobacter,* and *Pseudomonas* on a case-by-case basis.
- Per UCLA policy HS 1444, ID consult is required to use this drug.

Unacceptable uses

- Infections due to non-MDR pathogens for which alternate therapy, particularly beta-lactam antibiotics, are available
- Prophylaxis

Dose

5 mg/kg/day IV divided into 2-3 doses, adjust for renal function and dialysis (see Table)
75 mg inhaled q 12 hours

Toxicity

- Renal impairment, neuromuscular blockade, neurotoxicity
- Monitor serum creatinine a minimum of twice weekly.

Renal Function	**Loading Dose***	**Maintenance Dose***
CrCl > 50 mL/min	5mg/kg/dose x 1dose	2.5 mg/kg/dose-IV Q12H
CrCl: 20-50 mL/min	5mg/kg/dose x 1dose	2.5 mg/kg/dose-IV Q24H
CrCl: < 20 mL/min	5mg/kg/dose x 1dose	2.5 mg/kg/dose-IV Q48H
Intermittent hemodialysis	5mg/kg/dose x 1dose	30 mg-IV Q12H
Continuous renal replacement therapy	5mg/kg/dose x 1dose	100 mg-IV Q12H

*Use ideal body weight in obese patients

Daptomycin

ID consult or ASP approval is required

Daptomycin is a lipopeptide antibiotic. It has activity against most strains of staphylococci (including MRSA) and streptococci (including VRE). It has no activity against Gram-negative organisms. Daptomycin is inactivated by pulmonary surfactant and should NOT be used in cases of documented or suspected pneumonia or other pulmonary infections.

Acceptable uses

- Bacteremia or endocarditis caused by MRSA or methicillin-resistant coagulase-negative staphylococci in a patient with a serious allergy to vancomycin
- Therapy for MRSA infections (other than pneumonia) in which the MIC of vancomycin is ≥2 mcg/mL
- Bacteremia or endocarditis caused by MRSA in a patient failing vancomycin therapy defined as:
    - Clinical decompensation after 3-4 days
    - Failure to clear blood cultures after 7-9 days despite therapeutic vancomycin concentrations
    - Select cases in which the MIC of vancomycin is ≥ 2 mcg/ml
- Salvage therapy for VRE infections other than pneumonia, on a case-by-case basis

Unacceptable uses

- Treatment of pneumonia of any kind, as daptomycin is inactivated by pulmonary surfactant.
- Initial therapy for Gram-positive infections
- VRE colonization of the urine, respiratory tract, wounds, or drains
- Convenience due to ease of dosing compared to vancomycin. Clinical pharmacists and/or the Antimicrobial Stewardship Program pharmacists are available to assist with vancomycin dosing.

Dose

- Bacteremia: 6-10 mg/kg IV q24h
- Endocarditis: 6-10 mg/kg IV q24h
- Dose adjustment is necessary for renal replacement therapy and CrCl < 30 ml/min

Toxicity

- Myopathy (defined as CK more than 10 times ULN without symptoms or more than 5 times ULN with symptoms)
- Monitoring: total CK and creatinine weekly

Ertapenem

Ertapenem is a carbapenem antibiotic. Like the other carbapenems, ertapenem has *in vitro* activity against many Gram-negative organisms including those that produce extended spectrum beta-lactamases (ESBL). Importantly, it is not active against *P. aeruginosa* or *Acinetobacter* spp. The anti-anaerobic and Gram-positive of ertapenem activity is similar to the other carbapenems; one notable exception is that it is not active against *Enterococcus* spp.

Acceptable uses

- Mild to moderate intra-abdominal infections (biliary tract infections, diverticulitis, secondary peritonitis/GI perforation)
- Moderate diabetic foot infections
- Moderate surgical-site infections following contaminated procedures
- Urinary tract infections caused by ESBL-producing organisms
- Pyelonephritis due to ESBL-producing organisms
- Outpatient antibiotic therapy for patients requiring IV antibiotics for polymicrobial infections caused by susceptible organisms

Unacceptable uses

- Infections in which *Pseudomonas* spp. or *Acinetobacter* spp. are suspected

Dose

- 1 gm IV q24h.
- For dialysis-dependent patients and/or those with an estimated ClCr < 30 ml/min, use 500 mg q24.

Toxicity

- Diarrhea, nausea, headache, phlebitis/thrombophlebitis

Fidaxomicin

ID consult or ASP approval is <u>required with non-formulary request form</u>

Fidaxomicin is a macrocyclic antibiotic with narrow activity against Clostridium difficile (C diff). Unlike metronidazole and vancomycin, which are bacteriostatic, fidaxomicin is bactericidal. Fidaxomicin may cause less disruption of normal colonic flora (microbiome) than vancomycin or metronidazole. In a randomized controlled trial, clinical cure rates with fidaxomicin and vancomycin were similar, but recurrence of C difficile was less likely with fidaxomicin than with vancomycin in patients with non-NAP1 strains. Lower recurrence rates were not seen among patients with the NAP1 strain. Due to its extremely high cost, routine use of fidaxomicin is not recommended. Testing for NAP1 strains is not available routinely.

At UCLA Health, fidaxomicin requires Infectious Diseases consultation for use. Other options, such as fecal microbial transplant, may be preferable to treatment with fidaxomicin. Contact Dr. Dan Uslan for questions about fecal microbial transplant.

Acceptable uses:

- Treatment of C difficile infection in patients with recurrent infection who have failed treatment with vancomycin and metronidazole, and only with Infectious Diseases recommendation. Consider fecal microbial transplant as an alternative.

Unacceptable uses:

- Routine treatment of C difficile infection as initial therapy.

Fosfomycin

Fosfomycin is a synthetic, broad-spectrum, bactericidal antibiotic with *in vitro* activity against gram-negative and gram-positive organisms including *E. coli, Klebsiella spp, Proteus spp,* and vancomycin resistant *Enterococcus* (VRE). It does not have reliable activity against *Pseudomonas spp* or *Acinetobacter*. Fosfomycin is available in the US as an oral formulation only and its pharmacokinetics allow for one-time dosing.

Acceptable uses

- Management of uncomplicated UTI in patients with multiple antibiotic allergies and when oral therapy is indicated.
- Uncomplicated UTI due to VRE in patients with documented penicillin allergy.
- Salvage therapy for UTI due to multidrug-resistant organisms (e.g. ESBL, VRE, ±*Pseudomonas*) on a case by case basis.

Unacceptable uses

- Never use fosfomycin for management of infections outside the urinary tract because the oral formulation does not achieve adequate concentrations at other sites.

Dose

- Uncomplicated UTI: 3g (1 sachet) PO once.
- Complicated UTI (salvage therapy): 3g (1 sachet) PO every 3 days, up to 21 days.
- Powder should be mixed with 90-120 mL of cold water, stirred to dissolve and taken immediately. May be administered with or without food.

Toxicity

- Diarrhea, nausea, headache, dizziness, asthenia and dyspepsia

Antibiogram (2013)

Organism	Number of isolates	%S*	%I*	%R*
Escherichia coli	700	90.71%	5%	4.29%
Klebsiella pneumoniae	197	81.22%	9.64%	9.14%
Klebsiella oxytoca	21	100%	0%	0%
Proteus mirabilis	66	89.39%	6.06%	4.55%
TOTAL	984	88.92%	5.90%	5.18%

*Percentages calculated from AML ESBL Log
KEY: S = susceptible, I = intermediate, R = resistant

Isavuconazole:

ID consult or ASP approval is <u>required</u>
Formulations:

- Isavuconazonium Sulfate (Intravenous)
- Isavuconazole Sulfate (Oral)

Isavuconaole is a triazole antifungal used for the treatment of invasive aspergillosis and invasive mucormycosis. There are both IV and oral formulations, and they are bioequivalent. The IV formulation, Isavuconazonium sulfate, is the prodrug of isavuconazole. Isavuconazole treats

invasive fungal infections by inhibiting the synthesis of ergosterol, a key component of the fungal cell membrane, through the inhibition of cytochrome P-450 dependent enzyme lanosterol 14-alpha-demethylase. Given it utilizes this pathway, it has multiple drug-drug interactions, which should be checked prior to drug initiation. The drug is given with a loading dose, followed by maintenance therapy. Dose reduction for hepatic impairment is required. Common side effects including GI upset, elevated liver enzymes, cardiac and QTc abnormalities, hypokalemia, cough, and peripheral edema. It is contraindicated in familial short QT syndrome and strong inducers or inhibitors of CYP3A4.

Acceptable uses

- Treatment of invasive aspergillosis or invasive mucormycosis

Unacceptable uses:

- Any use in patients with familial short QT syndrome
- First line treatment of other fungal infections when other antifungal agents are available and susceptible

Linezolid

Linezolid is an oxazolidinone. It has activity against most strains of staphylococci (including MRSA), streptococci, and enterococci (including VRE). It does NOT have activity against Gram-negative organisms. It is available IV and PO and is 100% bioequivalent.

Acceptable uses

- Documented vancomycin-intermediate *Staphylococcus aureus* (VISA) or vancomycin-resistant *Staphylococcus aureus* (VRSA) infection.
- Documented MRSA or methicillin-resistant coagulase-negative staphylococcal infection in a patient with a severe allergy to vancomycin.
- Documented MRSA or methicillin-resistant coagulase-negative staphylococcal infection in a patient failing vancomycin therapy despite appropriate levels.
- Bacteremia/endocarditis: failure to clear blood cultures after 7-9 days despite vancomycin troughs of 15-20 mcg/mL or in a patient with a MRSA isolate with a MIC ≥ 2 mcg/ml. Should be used in combination with another agent as linezolid is bacteriostatic, not bactericidal.
- Pneumonia: worsening infiltrate or pulmonary status in a patient with documented MRSA pneumonia after 2-3 days of vancomycin therapy or if the MIC of vancomycin is ≥ 2 mcg/ml. ID consultation strongly advised.
- High suspicion of CA-MRSA necrotizing pneumonia in a critically-ill patient.
- Documented VRE infection (not colonization).
- Post-neurosurgical shunt infection, meningitis or ventriculitis due to *Staphylococcal spp* or VRE.
- Gram-positive cocci in chains in a blood culture in an ICU, solid oncology, or transplant patient known to be colonized with VRE.
- Treatment of atypical mycobacterial or nocardial infections on a case by case basis. ID consultation strongly advised.

Unacceptable uses

- Prophylaxis.
- Initial therapy for staphylococcal infection.
- VRE colonization of the stool, urine, respiratory tract, wounds, or drains

Dose

- 600 mg IV/PO q12h

Toxicity

- Bone marrow suppression (usually occurs after 10-14 days of therapy). Pyridoxine is of no benefit.
- Optic neuritis and irreversible sensory motor polyneuropathy (usually occurs with prolonged therapy >28 days)
- Lactic acidosis (case reports)
- Serotonin syndrome when co-administered with serotonergic agents e.g. SSRIs, SNRIs, TCAs, MAOIs (case reports)
- Monitoring: CBC weekly, consider periodic LFTs with prolonged use.

Polymyxin B (Intravenous)

ID consult or ASP approval is <u>required</u>

Polymyxin B is a polymyxin antibiotic. Similar to Colistin (polymyxin E), polymyxin B is a bactericidal agent that interacts with phospholipids of the bacterial cell membrane resulting in increased cellular permeability and cell death. Polymyxin B is active against aerobic Gram negative bacteria only (see Colistin section for details on spectrum of activity). Unlike Colistin, which is administered as the prodrug colistin methanesulfonate sodium (CMS) that is primarily eliminated by renal mechanisms, polymyxin B is administered as a positively charged sulfate salt (the active moiety) and undergoes primarily non-renal elimination. Thus, one therapeutic advantage of polymyxin B over Colistin is that the totally daily dose of polymyxin B is not affected by kidney function.

Given the high incidence of nephrotoxicity and neurotoxicity including paresthesia, dizziness, vertigo, ataxia, blurred vision, and slurred speech associated with parenteral administration of polymyxins compared to other available antibiotics, intravenous polymyxin B is reserved for serious infections with multi-drug resistant bacteria when all other alternative agents are contraindicated.

Acceptable uses:

- Management of infections due to multi-drug Gram negative pathogens on a case-by-case basis
- Per UCLA policy HS1444, formal ID consult is required to obtain Polymyxin B

Unacceptable uses:

- Infections due to non-MDR pathogens for which alternate therapy is available
- Prophylaxis

Quinupristin/dalfopristin (Synercid)

ID consult or ASP approval is <u>required</u>

Quinupristin/dalfopristin is an IV antibiotic for resistant gram-positive infections. It inhibits bacterial protein synthesis by binding to different sites on the 50S bacterial ribosomal subunit thereby inhibiting protein synthesis. It is FDA approved to treat complicated skin and soft tissue infections and has also been used off label for MRSA and VRE bacteremia/endocarditis. The drug has activity again vancomycin resistant *Enterococcus faecium*, but has poor activity to *Enterococcus faecalis*. The drug is limited by frequent and severe side effects that make the drug difficult to tolerate. There are also multiple CYP3A4 interactions.

Common Side Effects:

- Hyperbilirubinemia, GI upset, phlebitis/pain at infusion site [must be given with CVC], arthralgias, myalgias

At UCLA Health, use of quinupristin/dalfopristin requires Infectious Diseases consultation for use.

Acceptable Uses:

- Treatment of complicated VRE infections with E. faecium when no other agents are available
- Treatment of complicated MRSA infections when no other agents are available

Unacceptable Uses:

- Initial therapy for VRE, MRSA if another agent is available and susceptible
- Any infections with Enterococcus faecalis (has decreased activity)
- Patients without a CVC (given severe pain, phlebitis with infusions)
- Caution in patients with CYP3A4 drug interactions
- Any patient with a hypersensitivity to synercid

Aerosolized Ribavirin

ID consult or ASP approval is <u>required</u>

Ribavirin is a synthetic guanosine nucleoside analog. Ribavirin inhibits viral replication by interfering with synthesis of guanosine triphosphate thereby inhibiting nucleic acid synthesis. Ribavirin inhibits a wide range of RNA and DNA viruses including influenza A/B, respiratory syncytial virus (RSV), and parainfluenza.

Aerosolized ribavirin is approved for treatment of severe lower respiratory tract infections (LRTI) due to RSV in hospitalized children. It is often reserved for immunocompromised children with severe RSV LRTI. Both oral and inhaled ribavirin have been used to successfully treat immunocompromised adult patients with RSV pneumonitis. At UCLA, ribavirin is also used to treat immunocompromised adult patients with severe RSV disease.

Aerosolized ribavirin has been associated with mild conjunctival rash and irritation, dry cough, and dyspnea. When administered for short duration (< 5 days), hematologic toxicity is rare. Ribavirin is teratogenic and is contraindicated in pregnancy. Ribavirin exposure may occur in health care personnel working in the environment of an aerosolized-treated patient. To avoid exposing health care workers to the teratogenic effects of ribavirin, aerosolized ribavirin is administered either directly through the ventilator circuit (intubated patients) or via an oxygen hood; both methods require limited time in the room by health care providers to minimize exposure. In order to minimize health care worker exposure and optimize patient care, <u>inhaled ribavirin should be reserved for patients in whom oral ribavirin is contraindicated</u>.

Contraindications to oral ribavirin include: Hypersensitivity to ribavirin or any component of the formulation, patients with hemoglobinopathies (e.g. thalassemia major, sickle cell anemia), concomitant use with didanosine, renal insufficiency (CrCl < 50 ml/min) for the following oral preparations: Ribasphere capsules and Rebetol capsules/solution, and NPO status. Both aerosolized and systemic ribavirin are contraindicated in pregnant women and males who female partners are pregnant/planning to become pregnant.

Acceptable uses:

- Management of respiratory RSV infections in immunocompromised patients on a case-by-case basis in whom oral ribavirin is contraindicated.
- Per UCLA policy HS1444, formal ID consult is required to obtain inhaled ribavirin and the ordering provider is required to notify the Director of Safety at the time of prescription.

Unacceptable uses:

- Infections due to RSV in immunocompromised patients who can take ribavirin by mouth.

Tigecycline

ID consult or ASP approval is <u>required</u>

Tigecycline is a tetracycline derivative. It has *in vitro* activity against most strains of staphylococci, streptococci, and enterococci (including MRSA and VRE), anaerobes, and many gram-negative organisms with the exception of *Pseudomonas, Proteus, and Providencia*. It is FDA-approved for treatment of skin and skin-structure infections and intraabdominal infections. Tigecycline distributes extensively into tissues resulting in low peak serum concentrations, which limits its use for treatment of bloodstream infections.

FDA Black Box Warning [updated 9/2013]: Increased mortality risk associated with the use of the intravenous Tygacil (tigecycline) compared to that of other drugs used to treat a variety of serious infections: http://www.fda.gov/Drugs/DrugSafety/ucm224370.htm

Acceptable uses

- Management of intra-abdominal infections in patients with contraindications to both beta-lactams and fluoroquinolones.
- Management of infections due to multidrug resistant Gram-negative organisms including *Acinetobacter* on a case by case basis.
- Salvage therapy for MRSA or VRE infections on a case by case basis.

Unacceptable use

- Bacteremia and endocarditis.
- Tigecycline should not be used to treat pneumonia as unacceptably high failure rates have been reported (see black box warning).

Dose

- Usual dose: 100 mg IV once, then 50 mg IV q12h
- Severe hepatic impairment (Child Pugh Class C): 100 mg IV once, then 25 mg IV q12h

Toxicity

- Severe nausea/vomiting (most common), diarrhea (including *C. difficile*), abdominal pain, elevated liver transaminases, pancreatitis (acute)
- Monitoring: LFTs weekly

Vancomycin

At UCLA in 2014, 33% of all *S. aureus* isolates were resistant to oxacillin. These data suggest that empiric use of vancomycin is advisable for an ill patient with suspected *S. aureus* infection. However, <u>vancomycin should be stopped if culture data do not indicate a need for continued definitive therapy</u> (see below). **Limiting prolonged or inappropriate use of vancomycin is essential**. Presently vancomycin is the most highly utilized antibiotic at UCLA, with

approximately 15% of all inpatients receiving at least one day of therapy. There are few instances when continued use of vancomycin is appropriate in the absence of positive cultures. The following are recommendations for empiric, definitive, and prophylactic vancomycin therapy.

Acceptable Empiric Use

- Treatment of suspected community- or nosocomial-acquired bacterial meningitis.
- Treatment of healthcare-associated (including ventilator-associated) pneumonia.
- Treatment of peritoneal dialysis-related peritonitis in a severely ill patient.
- Treatment of sepsis in a patient at risk for MRSA bacteremia [catheter in place, indwelling hardware, known MRSA colonization, transfer from a nursing home or subacute facility, recent (within 3 months) or current prolonged hospitalization >2 weeks, hemodialysis].
- Treatment of surgical-site infection following placement of hardware.
- Treatment of severe diabetic foot infection in a patient at risk for MRSA.
- Treatment of necrotizing fasciitis.
- Treatment of suspected endocarditis in a moderately or severely ill patient after appropriate blood cultures are obtained.
- Treatment of Gram-positive cocci in clusters in ≥ 1 set of blood cultures in a moderately or severely ill patient.
- Treatment of Gram-positive cocci in clusters or chains in ≥ 2 sets of blood cultures in any patient.

Note: empiric therapy should be **discontinued** within 72 hours if criteria for definitive therapy (listed below) are **not** met:

Acceptable Use for Definitive Intravenous Therapy

- Proven infection with beta-lactam resistant organisms:
    - MRSA
    - Methicillin-resistant coagulase-negative staphylococcus
    - Ampicillin-resistant enterococcus (if susceptible)
    - Ceftriaxone-resistant *S. pneumoniae* (CSF only)
- Treatment of infections caused by Gram-positive organisms in patients who have severe allergic reactions to beta-lactam antibiotics (see discussion of penicillin allergy).

Acceptable Use for Definitive Oral Therapy

- *Clostridium difficile* infection (see CDI section)

Acceptable Use for Prophylaxis

- Prophylaxis for cardiac, vascular, or orthopedic (joint replacement, spinal fusion, ORIF only) surgery with a documented reason in the chart or in patients with severe beta-lactam allergy (no more than one pre-op and one post-op dose).

Unacceptable Uses for Vancomycin

- Continued empiric use for presumed infection with negative cultures.
- Treatment of a single-positive blood culture for coagulase-negative staphylococci.
- Routine surgical prophylaxis except as above.
- Empiric treatment for first fever in neutropenic patients without evidence of catheter-related bloodstream infection (e.g. inflamed IV catheter site), severe mucositis, or history of MRSA.

- Prophylaxis for infection or colonization of indwelling intravascular or intracranial catheters.
- Selective decontamination of the digestive tract.
- Eradication of MRSA colonization.
- Routine prophylaxis for patients on continuous ambulatory peritoneal dialysis or hemodialysis.
- When chosen only for convenience of dosing for treatment of infections caused by beta-lactam susceptible organisms in patients who are HD-dependent.
- Topical application or irrigation.

Dosing

- Round dose to nearest 250 mg increment
- Maximum: 2 gram/dose
- Trough levels should be obtained within 30 minutes before the 4th dose for a new regimen or dose change. Vancomycin troughs are not recommended if anticipated duration of therapy is ≤ 3 days.
- Goal trough concentrations:
    - Uncomplicated infections: skin/soft tissue infections, UTI: 10-15 mcg/mL.
    - Serious/Severe infections* (meningitis, endocarditis, BSI, PNA, osteo): 15-20 mcg/mL.

Renal Function	**Dose**
CrCl >60mL/min	<u>Uncomplicated Infections</u> 10-15mg/kg IV Q12h <u>Serious/Severe Infections*</u> Consider *loading dose* of 25mg/kg IV x1 followed by 15-20mg/kg IV Q8-12h
CrCl: 40-60 mL/min	10-15mg/kg IV Q12h-Q24h
CrCl: 20-40mL/min	5-10mg/kg IV Q24h
CrCl: 10-20 mL/min	5-10mg/kg IV Q24h-Q48h
CrCl: <10 mL/min	10-15mg/kg IV loading dose x1, then redoes according to levels
Intermittent hemodialysis	15-20mg/kg loading dose x1 followed by 0.5-1g PHD only
Continuous renal replacement therapy	10-15mg/kg IV Q24h

*ID consultation recommended
KEY: BSI: bloodstream infection, PNA: pneumonia, UTI: urinary tract infection