# INDICATIONS FOR APPROVAL/USE

| | | | |
|---|---|---|---|
| Ampicillin-Sulbactam (high dose) | Ceftolozane-Tazobactam | Meropenem and Ertapenem | Voriconazole |
| Amphotericin B | Colistin | Micafungin | Other |
| Artesunate | Dalbavancin | Polymyxin B | |
| Aztreonam | Daptomycin | Posaconazole | |
| Cefiderocol | Fidaxomicin | Sulbactam-Durlobactam | |
| Ceftaroline | Fosfomycin | Tedizolid | |
| Ceftazidime-Avibactam | Isavuconazole | Tigecycline | |

## Ampicillin-Sulbactam (High Dose)

***See XDR GNR Treatment Algorithm***

**Acceptable uses**

- Moderate-severe infections caused by Carbapenem-Resistant *Acinetobacter* (CRAB)
- May remain effective even if the isolate is ampicillin-sulbactam resistant
    - Should be used as a component of combination therapy

**Dosing**

- 9g (6g of ampicillin/3g of sulbactam) IV q8h infused over 4 hours
- Renal dose adjustments:

| Creatinine Clearance | Dosing |
|---|---|
| CrCl > 29 mL/min | 9g every 8 hours |
| CrCl 10-29 mL/min | 9g every 12 hours |
| CrCl < 10 mL/min | 9g every 24 hours |
| Hemodialysis (HD) | 9g every 24 hours |
| Continuous renal replacement therapy (CRRT) | 9g every 12 hours |

## Amphotericin B Liposomal (Ambisome®)

**Spectrum of Activity**

- Ambisome has broad antifungal coverage with in vitro activity against *Candida, Aspergillus*, dimorphic fungi, and some Zygomycetes (e.g. *Mucor*)
- Coverage gaps: *Candida lusitaniae, Aspergillus terreus, Scedosporium spp.,* and *Trichosporon* spp.

**Acceptable uses**

- Treatment:
    - Suspected or confirmed invasive Mucormycosis
    - Cryptococcal meningitis induction therapy
    - Candidal endophthalmitis, endocarditis
    - Fungal CNS disease
    - Severe dimorphic fungi infections

**Dosing**

- 3-5mg/kg IV q24h depending on organism and site of infection
    - 5mg/kg IV q24h is recommended for invasive or severe disease, endocarditis, meningitis
    - 5-10 mg/kg IV q24h for Mucormycosis
- Dose adjustments are not necessary in renal or liver dysfunction
- Premeds:
    - Acetaminophen 500mg PO q24h given 30 mins before infusion
    - Diphenhydramine 25mg IV q24h given 30 mins before infusion
    - Meperidine 25mg IV q24h given before infusion for 2 days and as needed for rigors thereafter
    - Normal saline 500 mL bolus before and after infusion

**Monitoring**

- Adverse Reactions: Nephrotoxicity, infusion-related reactions (flushing, urticaria, chills, rigors, chest pain, hypoxia, dyspnea, hypotension, abdominal pain), electrolyte abnormalities (notably, hypokalemia and hypomagnesemia), increase in LFTs
- Labs/Tests: CMP (including Mg) at baseline, daily while inpatient, at least every week after therapy and up to 3 times weekly as outpatient until stability demonstrated; may require significant repletion

**Notes**

- Ambisome and Amphotericin B deoxycholate are different preparations and have different dosing. Ambisome is preferred agent at VUMC.
- Ambisome should not be used for fungal UTIs. Amphotericin B deoxycholate is preferred.
- Electrolyte abnormalities can persist for ≥1 week after discontinuation and require continued monitoring until stable.
- Watch for additive renal dysfunction if patient is on other nephrotoxic medications (e.g. vancomycin, aminoglycosides, NSAIDs).

# Artesunate

**Acceptable uses**

- Severe malaria and/or patient is unable to tolerate oral medication
- Severe malaria defined as a positive blood smear in the presence of impaired consciousness/coma, hemoglobin < 7 g/dL, acute kidney injury, acute respiratory distress, circulatory collapse/shock, acidosis, jaundice (with other signs of severe malaria) disseminated intravascular coagulation, and/or parasite density of ≥ 5%

**Dosing**

- 2.4 mg/kg IV at 0, 12, and 24 hours, then once daily
- After 0-, 12-, and 24-hour doses, clinicians should either
    - A) Proceed with a full course of oral follow-on treatment as soon as parasite density ≤1% and the patient can tolerate oral medications.
        - For those patients with parasite density ≤1% but who still cannot tolerate oral medications after completing IV artesunate treatment, clinicians can continue IV artesunate, 1 dose daily not to exceed a total course of 7 days.
        - **Clinicians can consider the placement of a nasogastric tube or the use of antiemetics to facilitate the administration of oral treatment**
    - B) Continue IV artesunate treatment with the recommended dose once a day for a maximum of 7 days until parasite density is ≤1%

**Monitoring**

- Post artesunate delayed hemolysis
    - Can occur at least 7 days after initiating artesunate treatment.
    - Monitor patients for 4 weeks after treatment for signs of hemolytic anemia.

**Notes**

- Order has RedCap link for provider to confirm severe malaria diagnosis

# Aztreonam

***See B-lactam Cross Reactivity Chart** on VASP website

**Acceptable uses**

- Severe type I hypersensitivity reaction to beta-lactam antibiotics and no alternative beta-lactam based on side-chain cross-reactivity
- History of severe cutaneous adverse reaction (such as DRESS, SJS) to beta-lactam antibiotics
- In combination with avibactam for MBL-producing organisms

**Unacceptable uses**

- Reported PCN allergy (must get allergy details…)

- Availability of appropriate non-beta-lactam antibiotics

**Notes**

- Aztreonam is not as efficacious as beta-lactams against GNRs given empiric VUH susceptibilities
- Shares side chain with ceftazidime

## Cefiderocol

***See XDR GNR Treatment Algorithm***

**Spectrum of activity**

- Multi-drug resistant gram-negative bacteria, including bacteria producing ESBLs, AmpC, KPC, OXA-48, and metallo beta-lactamases (NDM, VIM); activity against some multi-drug resistant *Stenotrophomonas maltophilia*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*
- No clinically relevant in vitro activity against gram-positive or anaerobic bacteria

**Acceptable uses**

- Multi-drug resistant gram-negative infections with known sensitivity to cefiderocol
  *OR*
- Sepsis with history of documented carbapenem-resistant (CR) Enterobacterales NOT susceptible to ceftazidime-avibactam, CR *Pseudomonas* NOT susceptible to ceftazidime-avibactam or ceftolozane-tazobactam, CR *Acinetobacter*, MDR *Stenotrophomonas*

**Dosing**

| Creatinine Clearance | Dosing |
|---|---|
| >120 mL/min | 2g Q6h |
| 60-120 mL/min | 2g Q8h |
| 30-60 mL/min | 1.5g Q8h |
| 15-30 mL/min | 1g Q8h |
| CrCl < 15 mL/min | 750 mg Q12h |
| Hemodialysis (HD) | 750 mg Q12h |
| Continuous renal replacement therapy (CRRT) | Effluent flow rate ≤2 L/hour: 1.5 g Q12h<br>Effluent flow rate 2.1 to 3 L/hour: 2 g Q12h<br>Effluent flow rate 3.1 to 4 L/hour: 1.5 g Q8h<br>Effluent flow rate ≥4.1 L/hour: 2 g Q8h |

**Notes**

- Avoid use as monotherapy for CR *Acinetobacter* infections

# Ceftaroline

**Acceptable uses**

- Select cases of MRSA pneumonia or other severe infections when GNR coverage is also needed
- Bacteremia/endocarditis secondary to MRSA in patient failing vancomycin (see acceptable use for daptomycin)
- MRSA with vancomycin MIC ≥ 2 mcg/mL
- Daptomycin non-susceptible *Enterococcus* (in combination with daptomycin)

**Unacceptable uses**

- Treatment of CAP or SSTI (other more established and less expensive options available)
- Initial therapy for GPC or GNR infections

**Notes**

- Spectrum of activity is similar to ceftriaxone except with activity against MRSA; NO activity against ***Pseudomonas/Acinetobacter*** or gram-negative anaerobes
- Ceftaroline can cause false positive direct Coombs test without hemolytic anemia. If drug-induced hemolytic anemia is suspected, stop ceftaroline.

# Ceftazidime-Avibactam

***See XDR GNR Treatment Algorithm***

**Acceptable uses**

- Multi-drug resistant gram-negative infections with known susceptibility to ceftazidime-avibactam *OR*
- Empiric carbapenem-resistant (CR) Enterobacterales therapy with one of the following criteria:
    - Sepsis with history of documented CRE infection in the past 90 days
        - Prefer ceftolozane-tazobactam if prior history of CR *Pseudomonas*
    - KPC or OXA-48 Carbapenem-resistant Enterobacterales (CRE) septicemia as reported by ePlex®

**Contraindications**

- Severe cephalosporin allergy

**Dosing**

| Creatinine Clearance | Dosing |
|---|---|
| >50 mL/min | 2.5g Q8h |
| 30-49 mL/min | 1.25g Q8h |
| 10-29 mL/min | 0.94g Q12h |
| CrCl < 10 mL/min | 0.94g Q24h |

| | |
|---|---|
| Hemodialysis (HD) | 0.94g Q24h |
| Continuous renal replacement therapy (CRRT) | 1.25-2.5g Q8h |

**Notes**

- Ceftazidime-avibactam has minimal activity against anaerobes and gram-positive cocci. Add metronidazole for intra-abdominal infections or vancomycin if GPC activity is needed.
- Ceftazidime-avibactam is not expected to be active against *Acinetobacter* that is resistant to ceftazidime.

## Ceftolozane-Tazobactam

***See XDR GNR Treatment Algorithm***

**Acceptable uses**

- Multi-drug resistant *Pseudomonas* infections with known sensitivity to ceftolozane-tazobactam

  *OR*
- Empiric carbapenem-resistant (CR) Pseudomonal therapy with one of the following criteria:
  - Sepsis with a history of documented CR Pseudomonal infection in the past 90 days
    - Ceftazidime-avibactam (Avycaz®) is preferred for empiric CRE coverage otherwise
  - Carbapenem-resistant *Pseudomonas* bacteremia

**Contraindications**

- Severe piperacillin-tazobactam or cephalosporin allergy

**Dosing**

| Creatinine Clearance | Dosing |
|---|---|
| >50 mL/min | 3g Q8h |
| 30-49 mL/min | 1.5g Q8h |
| 10-29 mL/min | 750 mg Q8h |
| CrCl < 10 mL/min | 2.25 g x 1, then 450 mg Q8h |
| Hemodialysis (HD) | 2.25 g x 1, then 450 mg Q8h |
| Continuous renal replacement therapy (CRRT) | 1.5 g Q8h |

**Notes**

- Add metronidazole for intra-abdominal infections

# Colistin

***See XDR GNR Treatment Algorithm***

**Acceptable Uses**

- Treatment of multi-drug resistant GNR (e.g. *Acinetobacter/Pseudomonas*) infection resistant to most other tested antibiotics on case-by-case basis

**Dosing**

- Refer to International Consensus Guidelines on Polymyxins (Tsuji BT, Pogue JM, Zavascki AP, et al. International Consensus Guidelines for the Optimal Use of the Polymyxins. *Pharmacotherapy*. 2019;39(1):10-39.)
- Conversions
    - Colistimethate sodium 1 mg = ~12,500 units of colistimethate sodium
    - Colistimethate sodium ~2.4 mg = 1 mg of colistin base activity
    - 1 mg colistin base activity (CBA) = 30,000 IU colistimethate sodium

**Unacceptable uses**

- Monotherapy for GNR infections

**Notes**

- Polymyxin B is preferred over colistin due to more favorable pharmacokinetics and decreased potential to cause nephrotoxicity .
- **Colistin is preferred over polymyxin B to treat UTIs**.
- Colistin susceptibility testing is done automatically by VUH Micro Lab on GNR resistant to ≥3 antibiotic classes
- Colistin renal toxicity has been associated with prescriber error and incorrect dosing

# Dalbavancin

***See Dalbavancin Standard Operating Procedure*** on VASP website

**Acceptable uses**

- Infective endocarditis, joint infections, or osteomyelitis due to vancomycin-susceptible *Staphylococcus*, *Streptococcus*, or *Enterococcus* species
- Complicated *Staphylococcus aureus* bacteremia

**Eligible patients**

- Patients who elect to leave against medical advice with 7 – 14 days remaining of treatment
- Patients who are stable and medically ready for discharge but who would otherwise not be able to be discharged due to the need for IV antibiotics

**Unacceptable uses**

- Patients who are deemed suitable candidates for OPAT or oral antibiotics
- Patients with <7 days remaining of therapy
- Pregnant and/or nursing patients
- Patients with a history of anaphylaxis or delayed severe cutaneous reactions to dalbavancin, glycopeptides, or lipopeptides
- Patients with infected prosthetic material or hardware not removed
- Patients who do not have documented negative blood cultures
- Patients with central nervous system infections, including epidural abscesses or meningitis

**Number of doses**

- Patients who have 7 – 14 days remaining of therapy should receive one dose of dalbavancin
- Patients who have >14 days remaining of therapy should receive two doses of dalbavancin

**Dosing**

| | **Weeks Remaining in Treatment** | |
|---|---|---|
| **Creatinine clearance** | **< 2 Weeks** | **≥ 2 weeks** |
| **≥ 30 mL/min** | 1500 mg IV once | 1500 mg IV on days 1 and 8 |
| **< 30 mL/min** | 1500 mg IV once | 1500 mg IV on day 1 followed by 750 mg on day 8 |

**Notes**

- Two doses as above provides treatment for 6 weeks
- Requires VASP approval
- Requires ID consult
- Please contact ID PharmD to coordinate transitions of care (insurance benefits investigation, vial replacement, outpatient appointment, etc.)

## Daptomycin

**Acceptable uses**

- VRE treatment other than pneumonia (high risk Dapto-R; check MIC!)
- Bacteremia/endocarditis caused by MRSA in a patient failing vancomycin (**high risk of Dapto-R; check Dapto MIC!)
- MRSA with vancomycin MIC ≥ 2 mcg/mL
- Severe allergy or AE (anaphylaxis, SJS, DRESS) to vancomycin
- Documentation of urine eosinophils with definitive vancomycin as the cause
- Peripheral eosinophilia with definitive vancomycin as the cause

- Unable to establish a safe vancomycin regimen

**Unacceptable uses**

- Initial therapy for gram-positive infections in the absence of strong expectations of VRE
- VRE colonization of the urine, respiratory tract, wounds, or drains

**Dosing**

- Uncomplicated UTI or skin & soft tissue infection: 4 mg/kg
- Intra-abdominal infection or complicated skin & soft tissue infection: 8 mg/kg
- Osteomyelitis: 8-10 mg/kg
- Bacteremia, Endocarditis: 10 mg/kg
- **Dosing interval: q24h (extend to q48h for CrCl <30 mL/min)**
- **Note: for serious Enterococcus faecium infections, use 10-12 mg/kg**

**Notes**

- Daptomycin should not be used for treatment of primary lung infections (pneumonia/abscess). It may be used for empyema if no other alternatives are available.

## Fidaxomicin

**See C. diff algorithm on VASP website**

**Reason for Restriction**

- Cost; must make sure patient can obtain as an outpatient before starting inpatient

**Acceptable Uses**

- First occurrence for immunosuppressed patients
- First occurrence for immunocompetent patients with ≥3 risk factors (see VASP algorithm)
- First recurrence for immunocompetent patients

**Unacceptable Uses**

- C. diff. prophylaxis, including primary and secondary prophylaxis
- C diff. colonization (PCR+/toxin-)
- Fulminant disease

**Dosing**

- See VASP algorithm

# Fosfomycin

**Acceptable Uses**

- Treatment of cystitis due to multi-drug resistant *E. coli* and GPCs (including VRE)

**Unacceptable uses**

- Infections outside the urinary tract (poor tissue penetration, including pyelonephritis)
- Should not be used for K*lebsiella pneumoniae* due to fosA gene which may lead to clinical failure

**Dosing**

- Uncomplicated cystitis: 3g x 1
- Complicated cystitis or prostatitis: 3g Q24-48h (reserve for when there are no other options)

**Notes**

- Unusual formulation/dosing susceptible to dosing errors
- Should only be used for cystitis
- Susceptibility to fosfomycin should be confirmed prior to use
    - No breakpoints for *E. faecium*
- No *Acinetobacter* activity
- PO formulation only, IV formulation not available in the US
- Usually last-line option

# Isavuconazonium sulfate

**Spectrum of Activity**

- Broad coverage against *Candida, Aspergillus*, dimorphic fungi, *Fusarium* spp., as well as Zygomycetes (e.g. *Mucor*)

**Acceptable uses**

- Mucormycosis
    - Sequential therapy following induction with Amphotericin B
- Treatment or prophylaxis of invasive fungal infections in patients with an absolute contraindication to other azoles
    - Prolonged QTcF > 500
    - Interactions: sirolimus, arsenic
    - Inclusion in a clinical trial prohibiting strong CYP3A4 inhibitors
- Treatment or prophylaxis of invasive fungal infections in patients with a relative contraindication to other azoles
    - Apixaban for treatment of VTE
    - Amiodarone in combination with a QTcF >450
    - Other drug interactions can be considered on a case-by-case basis based on risk vs. benefit

- Unable to tolerate posaconazole or voriconazole

**Unacceptable uses**

- Should be avoided in pregnancy

**Requirements**

- A test claim must be processed in all new starts to ensure the patient will be able to afford isavuconazonium sulfate on discharge

**Dosing**

- Mucormycosis/aspergillosis
  - Loading dose: 372 mg IV/PO q8h x 6 doses
  - Maintenance dose: 372 mg IV/PO q24h (beginning 12-24 hrs after loading dose)
- 372 mg isavuconazonium sulfate = 200mg isavuconazole
- Formulations:
  - Capsule
    - Highly bioavailable. Absorption is not impacted by acid or food.
  - IV
    - No cyclodextrin
- Dose Adjustments:
  - Renal: no dosing adjustments recommended

**Monitoring**

- Adverse Reactions: Nausea, vomiting, diarrhea, elevated LFTs, shortened QTc
- Labs/Tests: AST/ALT at baseline and every 1-2 weeks after, baseline ECG
- Drug interactions: As a CYP-enzyme inhibitor and substrate, isavuconazole has drug interactions including oral anticoagulants, anti-epileptics, antiarrhythmics, SSRIs, antipsychotics, and immunosuppressants.

## Meropenem and Ertapenem

**Acceptable uses**

- Treatment of MDR GNR when:
  - Susceptibility to few or no traditional agents
  - Patient intolerant/has contraindications to other agents (other beta-lactams, fluoroquinolones)

**Unacceptable uses**

- Continuation of empiric treatment for when microbiologic results show susceptibility to other agents that are appropriate alternatives

- Empiric use in patients lacking risk factors for MDR GNR

**Note**s

- Meropenem and ertapenem are not restricted in the ICUs or in ED patients going to an ICU (for meropenem only) for the first 72 hours of use. Continuation after that time point will require ID approval via second sign process.
- Ertapenem does not have *Pseudomonas/Acinetobacter/Enterococcus* coverage
- Contraindicated with valproic acid and derivatives due to significant drug-drug interactions (decreased concentration of valproic acid) which is not minimized with dosage increases

## Micafungin

**Spectrum of Activity:**

- Micafungin has activity against *Candida spp*., including *C. glabrata,* and *C. krusei*
- Minimal activity against *Aspergillus spp*. has been demonstrated in vitro. This agent should not be used as monotherapy for this pathogen.

**Acceptable uses**

- Prophylaxis (per heme/SCT SOPs)
- Treatment
    - Candidemia and invasive candidiasis
    - *C. krusei or glabrata* candidiasis
- Azole intolerance:
    - Elevated LFTs (AST and ALT > 3x upper limit of normal)
    - Required by clinical trial protocol
    - Significant drug interaction
    - Prolonged QTc > 500
- Febrile neutropenia ≥ 96 hrs on appropriate therapy
- Prolonged neutropenia > 10 days
- Increased risk of veno-occlusive disease in stem cell transplant (start of conditioning through engraftment)

**Unacceptable uses**

- First line for aspergillosis or mucormycosis
- CNS infections or UTI (poor penetration)

**Dosing**

- Prophylaxis
    - Neutropenia (alternate): 50-100 mg IV daily
- Treatment
    - Candidiasis: 100mg IV daily

    - Esophageal candidiasis or *Candida* endocarditis: 150mg IV daily
- Dose Adjustments:
    - No dosing adjustments are recommended for renal or hepatic impairment

**Monitoring**

- Labs/Tests: AST/ALT at baseline and every 1-2 weeks after

## Polymyxin B

***See XDR GNR Treatment Algorithm***

**Acceptable Uses**

- Treatment of multi-drug resistant GNR (e.g. *Acinetobacter/Pseudomonas*) infection resistant to most other tested antibiotics on case-by-case basis

**Unacceptable uses**

- Monotherapy for GNR infections
- Safety in pregnant patients is not established

**Dose**

- Loading Dose: 20,000-25,000 IU/kg over 1 hour
- Maintenance Dose: 12,500-15,000 IU/kg every 12 hours infused over 1 hour

**Notes**

- May cause nephrotoxicity and neurotoxicity can result in respiratory paralysis when drug is given soon after anesthesia or muscle relaxants (Boxed Warnings)
- **Polymyxin B is general preferred over colistin except when treating UTIs**

## Posaconazole

**Spectrum of Activity:**

- Posaconazole has broad coverage against *Candida, Aspergillus*, dimorphic fungi, *Fusarium spp.*, as well as Mucorales

**Acceptable uses**

- Prophylaxis
    - AML induction, GVHD with high dose steroids (≥20mg/d prednisone) (Oncology pharmacist may bypass second sign when used for prophylaxis)
    - Post-lung transplant (Solid organ transplant pharmacist may bypass second sign when used for prophylaxis)

- Treatment
    - Aspergillosis
    - Dimorphic fungi infection or candidiasis in patients unable to take standard therapy
    - Mucorales maintenance therapy after infection has been controlled with amphotericin B +/- surgery

**Unacceptable uses**

- Should be avoided in pregnancy

**Dosing**

- Tablets: 300mg Q12h x 2 doses followed by 300mg daily
- IV: 300mg Q12h x 2 doses followed by 300mg daily
- Suspension: 200mg three to four times daily (not preferred due to unpredictable and variable absorption)

**Therapeutic Drug Monitoring**

- Obtain trough level 7 days after initiation of therapy
    - Goal trough: ≥0.7 (prophylaxis); ≥1 mcg/ml (treatment)
- Dose Adjustments:
    - No dosing adjustments recommended for renal or hepatic impairment though caution is warranted for IV therapy when CrCl < 50 ml/min

**Formulations**

- Delayed Release Tablet (preferred)
    - Administer after a meal (less dependent on food than suspension)
- Intravenous
    - Contains cyclodextrin, which may accumulate in renal dysfunction
- Suspension
    - Administer after high-fat, acidic meal (e.g. coke float)

**Monitoring**

- Adverse Reactions: Nausea, abdominal discomfort, elevated LFTs, prolonged QTc
- Labs/Tests: AST/ALT at baseline and every 1-2 weeks after, baseline ECG, renal function (IV only)
- Drug interactions: As a CYP-enzyme inhibitor and p-gp inhibitor/substrate, posaconazole has significant drug interactions including oral anticoagulants, anti-epileptics, anti-arrhythmics, SSRIs, antipsychotics, and immunosuppressants. Concurrent treatment with vinca alkaloids should be avoided.

## Sulbactam-Durlobactam

**Acceptable uses**

- Suspected or confirmed carbapenem-resistant *Acinetobacter* infections

**Dosing**

| Dose | CrCl (mL/min) | Frequency |
|---|---|---|
| sulbactam 1g and durlobactam 1g | ≥130 | Every 4 hours |
| | 45-129 | Every 6 hours |
| | 30 to 44 | Every 8 hours |
| | 15 to 29 | Every 12 hours |
| | <15 | Every 12 hours for first 3 doses, then every 24 hours |

**Notes**

- Studied in combination with carbapenem

## Tedizolid

**Acceptable uses**

- Gram-positive infections where IV antibiotics are not necessary and patient has allergies, drug interactions, or resistance to other oral options

**Notes**

- Tedizolid should NOT be used for febrile neutropenia (requires neutrophils to be active) or UTIs
- Need to make sure patient can afford (expensive)

## Tigecycline

***See XDR GNR Treatment Algorithm***

**Acceptable uses**

- As part of a combination regimen for NTM infection
- Treatment of MDR GNR when:
    - Pathogen is susceptible to few or no other agents
    - Patient intolerant/has contraindications to other agents (beta-lactams, fluoroquinolones, aminoglycosides)

**Dosing**

- 100 mg IV x 1, then 50 mg IV Q12h
- CRE, *Acinetobacter*, *S. maltophilia*: 200 mg IV x 1, then 100 mg IV Q12h

**Notes**

- Significant nausea/vomiting
- Tigecycline susceptibility testing is done automatically by VUH Micro Lab on GNR resistant to ≥3 antibiotic classes
- Avoid Tigecycline in pregnancy (Category D)
- Should not be used for treatment of bacteremia (low serum bioavailability, increased mortality in bacteremia)

## Voriconazole

**Spectrum of Activity:**

- Broad coverage against *Candida, Aspergillus*, dimorphic fungi, *Fusarium spp*.

**Acceptable uses**

- Treatment
    - Aspergillosis, Candidiasis (krusei)
    - Dimorphic fungal infections in patients unable to take standard therapy
    - Fusarium
- Prophylaxis
    - Post-lung transplant, heme malignancy, or post-stem cell transplant

**Unacceptable uses**

- Should be avoided in pregnancy

**Dosing**

- IV: 6 mg/kg Q12h x 2 doses then 3 mg/kg Q12h (adjusted body weight for obese)
- PO: 200-300 mg Q12h
- Dose adjusted based on troughs

**Dose Adjustments**

- Caution is warranted for prolonged use of IV therapy when CrCl < 50 ml/min
- Child-Pugh class A or B: consider reducing maintenance dosage by 50%
- Child-Pugh class C: consider benefits vs. risks

**Therapeutic Drug Monitoring**

- Obtain trough level 5-7 days after initiation of therapy
    - Goal trough: >1 mcg/ml (prophylaxis); 1-5.5 mcg/ml (treatment)

**Monitoring**

- Adverse Reactions: Elevated LFTs, prolonged QTc, visual changes, visual hallucinations, photosensitivity, squamous cell carcinoma with prolonged use
- Labs/Tests: AST/ALT at baseline and every 1-2 weeks after, baseline ECG, renal function (IV only)
- Drug interactions: As a CYP-enzyme inhibitor and substrate, voriconazole has significant drug interactions including oral anticoagulants, anti-epileptics, antiarrhythmics, SSRIs, antipsychotics, and immunosuppressants.

## Other Restricted Antimicrobials

- **Bedaquiline**:
    - Reason for restriction: Only indicated for the treatment of multi-drug-resistant tuberculosis for which alternative agents are ineffective
    - Consult TB experts prior to use
- **Chloramphenicol:**
    - Reason for restriction: Chloramphenicol associated with aplastic anemia
    - Indications for use: Few indications exist; most experts prefer doxy for tick-borne illnesses, even in pregnancy
- **Imipenem-cilastatin:**
    - Other carbapenems are available on formulary
    - Indications for use: Treatment of Nocardia and nontuberculous mycobacteria infections
- **Inhaled Ribavirin:**
    - Nonformulary; every request is reviewed by PT&D committee
    - PO ribavirin is on formulary
- **Moxifloxacin:**
    - Reason for restriction: Other quinolones are readily available on formulary
    - Indications for use: Treatment of certain mycobacterial infections, open globe prophylaxis
- **Quinine/Quinidine:**
    - Reason for restriction: Due to hematologic side effects
    - Quinine is not recommended for treatment of leg cramps
    - Indications for use: Serious infection with malaria.