LPCHS Antimicrobial Therapy Monitoring Guideline

Guideline Overview

This document is intended to guide laboratory test monitoring for patients receiving enteral and/or parenteral antimicrobials. The provided recommendations are derived from professional society guidelines (e.g., Infectious Diseases Society of America, American Academy of Pediatrics), drug package insert information, and published data.

The monitoring frequencies recommended within the table are the minimum criteria for safety monitoring for patients with normal baseline labs, hemodynamic stability, and stable organ function. More frequent monitoring may be needed based on patient characteristics, provider discretion, or upon consultation with Pediatric Infectious Diseases or the Antimicrobial Stewardship Program (ASP). Some antimicrobial agents have not been included due to infrequent use at Lucile Packard Children's Hospital Stanford (LPCHS) or in pediatric patients in general. Please see additional information available in the LPCHS Housestaff Manual and the IDSA OPAT Guideline. Consider change to enteral antimicrobials when clinically appropriate.

LPCHS Companion Guidelines available in the LPCHS Housestaff Manual and on the ASP website:

Aminoglycoside Dosing and Monitoring Guideline

Antimicrobial Renal Dose Adjustment Guideline

Azole Antifungal Therapeutic Drug Monitoring Guidance

Prolonged Infusion of Beta-Lactam Guideline

Vancomycin Dosing Guidelines: Guideline for Neonates and Children, Guideline for Obstetric Patients, Guideline in Hemodialysis

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Recommendations for Select Antimicrobial Agent Monitoring

The following laboratory monitoring guidance is intended for patients who do not have underlying risk factors for hematologic, renal, or hepatic toxicities. Many drug-induced laboratory abnormalities are either transient, clinically insignificant, and/or have onset after 1-2 weeks, by which time, patients may be approaching the end of their intended therapy.

Antimicrobial	Monitoring Frequency[a]	Common Potentially Serious ADRs (alphabetically)	Other Comments
Antibiotics			
Aminoglycosides			
Amikacin Gentamicin Tobramycin	**SCr/BUN** twice weekly for potential nephrotoxicity as well as potential need for renal dose adjustment.[b] **TDM:** For more information on timing of serum levels and goals refer to Aminoglycoside Guideline**.** **Clinical monitoring for vestibular and hearing dysfunction:** Consider audiometry for exposures > 7 days. Consider mitochondrial variant testing for prolonged courses. Outpatient: Patients should be tested before, during (at each clinic visit), and after treatment, particularly in those at risk for ototoxicity or those on prolonged therapy (> 14 days). **Outpatient:** Recommend at least weekly trough concentrations. More frequent monitoring and/or additional serum concentrations may be indicated based on changes in renal function or signs of toxicity.	**Nephrotoxicity**[c] **Neuromuscular blockade**: neurotoxicity (twitching, numbness, seizure, tingling of skin) **Ototoxicity**: Cochlear ototoxicity (i.e., auditory impairment, hearing loss, tinnitus – more with amikacin) Vestibular ototoxicity (i.e., dizziness, balance loss – more with gentamicin and tobramycin)	Hearing loss is associated with persistently elevated serum concentrations; early ototoxicity usually affects high-pitched sounds. Use with caution in patients with neuromuscular disorders, including myasthenia gravis.
Beta-lactams			
Ampicillin Ampicillin-sulbactam	Consider **CBCd** at baseline and every 2 weeks in patients with prolonged therapy (>14 days). **SCr/BUN** at baseline and as needed if concerned for renal impairment for assessment of renal dose adjustment.[b] **PT/INR** if on warfarin concurrently.	Hematologic abnormalities (rare); hypersensitivity, including anaphylaxis[d]	
Amoxicillin Amoxicillin-clavulanate	No routine laboratory monitoring. Consider **CBCd** after 4-6 weeks. Monitor **PT/INR** if on warfarin concurrently.	Hematologic abnormalities with prolonged therapy (thrombocytopenia, leukopenia, neutropenia); hypersensitivity, including anaphylaxis[d]	
Aztreonam	**LFTs**[e] weekly. **SCr/BUN** at baseline and as needed if concerned for renal impairment for assessment of renal dose adjustment.[b]	Hepatotoxicity (increased risk with doses of ≥ 200 mg/kg/day)[f]	Can be used for gram-negative coverage in all patents with a penicillin or cephalosporin allergy except in those with a ceftazidime allergy, as they share a similar side chain.
Cefazolin	Consider **CBCd** and **LFTs**[e] at baseline and every 2 weeks in patients with prolonged therapy (>14 days). **SCr/BUN** at baseline and as needed if concerned for renal impairment for assessment of renal dose adjustment.[b] **PT/INR** if on warfarin concurrently.	Hemolytic anemia (rare); hypersensitivity, including anaphylaxis[d]; LFT abnormalities[f]	

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Antimicrobial	Monitoring Frequency[a]	Common Potentially Serious ADRs (alphabetically)	Other Comments
Cefepime	Consider monitoring **CBCd** and **LFTs**[e] at baseline and weekly in patients with prolonged therapy (>14 days). **SCr/BUN** at baseline and as needed if concerned for renal impairment for assessment of renal dose adjustment.[b] **PT/INR** if on warfarin concurrently.	Hematologic abnormalities (rare); hypersensitivity, including anaphylaxis[d]; LFT abnormalities[f]; neurotoxicity (see comments)	Patients with renal insufficiency may be at increased risk for neurotoxicity, including seizures, encephalopathy, and asterixis. Use caution in patients with history of seizure disorder, particularly with renal impairment.
Cefdinir	No routine laboratory monitoring. Consider **CBCd** after 4-6 weeks. Monitor **PT/INR** if on warfarin concurrently.	Hematologic abnormalities with prolonged therapy (thrombocytopenia, leukopenia, neutropenia); hypersensitivity, including anaphylaxis[d]	Cefdinir may cause reddish stools when used concomitantly with iron-containing products due to formation of nonabsorbable complexes in the GI tract.
Cefixime			
Cefoxitin	Consider **CBCd** at baseline and every 2 weeks in patients with prolonged therapy (>14 days). **SCr/BUN** at baseline and as needed if concerned for renal impairment for assessment of renal dose adjustment.[b] **PT/INR** if on warfarin concurrently.	Hematologic abnormalities (rare); hypersensitivity, including anaphylaxis[d]	
Ceftaroline (NF)		Hypersensitivity, including anaphylaxis[d]; neurotoxicity (see comment); neutropenia (increased with use of higher than FDA approved doses in adults and prolonged use [>14 days])	Use caution in patients with history of seizure disorder, particularly in presence of renal impairment.
Ceftazidime		Hematologic abnormalities (rare); hypersensitivity, including anaphylaxis[d]; neurotoxicity	
Ceftazidime-avibactam (R)			
Ceftolozane-tazobactam (NF)	Consider **CBCd** weekly in pediatric patients (thrombocytopenia). **SCr/BUN** at baseline and as needed if concerned for renal impairment for assessment of renal dose adjustment.[b] **PT/INR** if on warfarin concurrently.	Hypersensitivity, including anaphylaxis[d]	
Ceftriaxone	Consider **CBCd** and **LFTs**[e] at baseline and every 2 weeks in patients with prolonged therapy (>14 days). **PT/INR** if on warfarin concurrently.	Hemolytic anemia (rare); hyperbilirubinemia (potential for kernicterus and bilirubin encephalopathy in neonates – see comment); hypersensitivity, including anaphylaxis[d]; LFT abnormalities[f]	Neonates should not receive ceftriaxone if they also are receiving, or are expected to receive, IV calcium in any form, including parenteral nutrition. Do not use in hyperbilirubinemic neonates and/or neonates <41 weeks postmenstrual age.
Cephalexin	No routine laboratory monitoring. Consider **CBCd** after 4-6 weeks. Monitor **PT/INR** if on warfarin concurrently.	Hematologic abnormalities with prolonged therapy (thrombocytopenia, leukopenia, neutropenia); hypersensitivity, including anaphylaxis[d]	

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Ertapenem (NF) Imipenem-cilastatin (NF) Meropenem	Consider **CBCd** and **LFTs**[e] at baseline and every 2 weeks in patients with prolonged therapy (> 14 days). **SCr/BUN** at baseline and as needed if concerned for renal impairment for assessment of renal dose adjustment.[b] **PT/INR** if on warfarin concurrently.	CNS effects (delirium and seizure – see comment); hematologic abnormalities (rare); hypersensitivity, including anaphylaxis[d]; LFT abnormalities[f]	Concurrent use with valproic acid and derivates or ganciclovir/valganciclovir (imipenem-cilastatin only) is **not** recommended due to increased risk of breakthrough seizure. If therapy necessary, valproic serum concentration monitoring and dose adjustment may be needed.
Nafcillin	Monitor **CBCd, electrolytes (K),** and **LFTs**[e] baseline and weekly. **SCr/BUN** weekly due to potential nephrotoxicity as well as potential need for renal dose adjustment.[b] **PT/INR** if on warfarin concurrently.	Hematologic abnormalities (agranulocytosis and bone marrow depression); hepatotoxicity[f]; hypersensitivity, including anaphylaxis[d]; hypokalemia; nephrotoxicity (interstitial nephritis)[c], neurotoxicity (i.e., seizure) with large IV doses of nafcillin especially in patients with concomitant hepatic insufficiency and renal dysfunction	Given increased risk for phlebitis, administration via central line is preferred.
Penicillin G (aqueous, IV) and Penicillin V potassium (enteral)	**IV: CBCd** and **electrolyte monitoring (Na**) at baseline and then once to twice weekly (see comment). Daily monitoring of potassium is recommended for the first 3-4 days of therapy, then spaced to twice weekly for 1 week, then weekly if stable (see comment). In patients on prolonged therapy (> 14 days), monitoring can be spaced to every 1-2 weeks in patients with stable laboratory markers. Additional clinical monitoring for symptoms of hyperkalemia (e.g., palpitation, muscle weakness or paralysis, or ECG changes) is also recommended. **SCr/BUN** at baseline and as needed if concerned for renal impairment for assessment of renal dose adjustment.[b] **PT/INR** if on warfarin concurrently. **PO:** No routine laboratory monitoring. Monitoring **PT/INR** if on warfarin concurrently.	Hypersensitivity, including anaphylaxis[d]; **IV:** Electrolyte imbalances (hypernatremia and hyperkalemia) at higher doses (e.g., >10 million units) (see other comments column); neurotoxicity (risk increased with renal dysfunction); neutropenia	Patients with renal impairment or those receiving large doses of IV penicillin G (e.g., >200,000 units/kg/day in children or >10 million units/day in adult patients) are at increased risk of serious and even fatal electrolyte disturbances. IV penicillin G contains 1.7 mEq of potassium per million units. Patients receiving doses of ≥44,000 units/kg of penicillin IV should have their infusion slowed to 30 mins, and doses ≥88,000 units/kg slowed to 60 minutes. Alternatively, patients total daily dose may be given as continuous infusion over 24hrs.
Piperacillin-tazobactam	Consider **CBCd** and **electrolyte monitoring (Na, K, Ca)** at baseline and every 2 weeks in patients with prolonged therapy (> 14 days). **SCr/BUN** weekly due to potential nephrotoxicity when concomitantly used with other nephrotoxins (e.g., vancomycin), as well as potential need for renal dose adjustment (see comment).[b] **PT/INR** if on warfarin concurrently.	Electrolyte derangements (Na, K, Ca); hematologic effects (myelosuppression, drug-induced immune thrombocytopenia); hypersensitivity, including anaphylaxis[d]; nephrotoxicity[c] (see comment); neurotoxicity (rare)	Recent studies have not found a significant difference in kidney injury between patients receiving piperacillin-tazobactam (pip-tazo) and those on alternative treatments.[9] New literature suggest that pip-tazo is a pseudonephrotoxin, causing changes in lab values without actual kidney damage.[10]

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Fluoroquinolones			
Ciprofloxacin Levofloxacin Moxifloxacin (NF)	No routine laboratory monitoring. Consider **LFTs**[e] at baseline and then every 2 weeks for patients on prolonged therapy (>14 days). Monitor for signs and symptoms of abnormalities in **glucose regulation** (especially in patients with diabetes mellitus). Consider **ECG** prior to initiation if history of elevated QTc or on other potential QTc prolonging medication and repeat ECG 2-3 days after initiation of other QTc prolonging medication.	Aortic aneurysm/aortic dissection; arthropathy/arthralgia; CNS effects; glucose dysregulation; hepatotoxicity[f]; peripheral neuropathy; phototoxicity/photoallergy; tendonitis/tendon rupture; known risk for TdP[g]	Refer to HSM monograph for timing of administration for food or medications containing calcium, iron, or zinc.
Macrolides			
Azithromycin Clarithromycin (NF) Erythromycin	No routine laboratory monitoring. Consider **LFTs**[e] at baseline and then every 2 weeks for patients on prolonged therapy (>14 days). Obtain **ECG** prior to initiation if history of elevated QTc or on other potential QTc prolonging medication and repeat ECG 2-3 days after initiation of other QTc prolonging medication.	Hepatotoxicity[f]; hypersensitivity, including anaphylaxis[d] and delayed (SJS/TEN); ototoxicity (hearing loss and tinnitus) with high dose (see comment); possible risk TdP[g]	Ototoxicity has been reported in those receiving 4g/day of IV erythromycin and in patients receiving daily oral azithromycin in doses of ≥ 500 mg.[11]
Tetracyclines			
Doxycycline Minocycline (NF)	No routine laboratory monitoring. Consider **LFTs**[e] at baseline and then every 2 weeks for patients on prolonged therapy (> 14 days) or in patients at increased risk for hepatotoxicity.[h] May reduce to monthly monitoring based on patient's tolerance and anticipated duration of patient therapy.	Bone growth suppression; esophageal injury; hepatotoxicity[f]; photosensitivity May induce **diffuse skin hyperpigmentation** including nails, skin of hands, arms, legs, dorsal side of feet, interdigital areas, or around scars. Risk of **dental staining** and **enamel hypoplasia** with doxycycline during tooth development is controversial; short-term use (<21 days) in children regardless of age is likely safe.[12]	Counsel on importance of sun avoidance, sun-protective clothing, and broad-spectrum sunscreen (UVA and UVB). Refer to HSM monograph for timing of administration for food or medications containing calcium, iron, magnesium, or zinc.
Miscellaneous			
Clindamycin	No routine laboratory monitoring. Consider **LFTs**[e] after 4-6 weeks in patients on prolonged therapy.	Antibiotic associated diarrhea, *Clostridioides difficile* infection; hepatotoxicity[f]	
Colistin, colistimethate (NF)	**SCr/BUN** twice weekly due to potential nephrotoxicity as well as potential need for renal dose adjustment (see comment).[b] Monitor for signs of neurotoxicity - IV doses > 5 mg CBA/kg/day are associated with increased incidence.[13]	Nephrotoxicity[c]; neurotoxicity (e.g., neuromuscular blockade which may cause apnea and respiratory arrest)	Consider more frequent monitoring of renal function if patients have signs indicating development of impaired renal function.[c]
Daptomycin (NF)	**Monitor CPK** at baseline and weekly. More frequent monitoring is recommended when daptomycin is used with concurrent statin therapy and/or renal impairment due to increased risk of muscle toxicity.	Eosinophilic pneumonia; myopathy; peripheral neuropathy; rhabdomyolysis	

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Antimicrobial	Monitoring Frequency[a]	Common Potentially Serious ADRs (alphabetically)	Other Comments
Linezolid (R)	**Monitor CBCd** at baseline and every 2 weeks for the first month, then monthly thereafter if on long-term therapy. Monitor for optic neuritis with visual exam and neuropathy with prolonged use (≥ 28 days).	Hematologic abnormalities (thrombocytopenia, leukopenia, anemia) peripheral neuropathy; optic neuritis; serotonin syndrome (e.g., agitation, confusion, hallucinations, hyperreflexia, myoclonus, shivering, tachycardia)	Caution with prolonged therapy due to increased risk of ADR, including myelosuppression (≥14 days) and peripheral/optic neuropathy (≥28 days).
Metronidazole	No routine laboratory monitoring. Consider **ECG** prior to initiation if history of elevated QTc or on other potential QTc prolonging medication and repeat ECG 2-3 days after initiation of other QTc prolonging medication.	Mental status changes; peripheral neuropathy; conditional risk for TdP[g]	Causes a bitter, metallic taste in mouth of ~10% of patients, which typically resolves in 1-2 days after finishing the medication.
Sulfamethoxazole-trimethoprim	Monitor **CBCd** and **electrolytes (Na, K, glucose**) weekly. **SCr/BUN** weekly due to potential nephrotoxicity as well as potential need for renal dose adjustment.[b] Transition to a reduced monitoring frequency (i.e., every other week or monthly labs) may be appropriate for patients on longterm prophylaxis. Routine **LFT** monitoring is not required but should be considered in patients showing signs of hepatotoxicity.[f] Consider **ECG** prior to initiation if history of elevated QTc and on other potential QTc prolonging medication and repeat ECG 2-3 days after initiation of other QTc prolonging medication.	Drug-induced liver injury[f] (most onset within 1-3 weeks); electrolyte imbalance (hyperkalemia, hypoglycemia, hyponatremia); hematologic abnormalities (agranulocytosis, hemolytic anemia, leukopenia, thrombocytopenia); hypersensitivity reaction, delayed (SJS/ TEN); nephrotoxicity[c]; rash; possible risk TdP[g]	Contraindicated in infants < 4 weeks; potential for drug-drug interactions; parenteral formulation is a large fluid volume. **Cross-reactivity:** The potential for cross-reactivity between antibiotic sulfonamides and nonantibiotic sulfonamides is extremely low. In patients with serious reactions (e.g., SJS/TEN, DRESS), consider avoiding all sulfonamide medications.[14]
Tedizolid (NF)	**Monitor CBCd** at baseline and every 2 weeks thereafter if on long-term therapy. Monitor for neuropathy with prolonged use (>14 days).	Hematologic abnormalities (neutropenia, thrombocytopenia); peripheral neuropathy	Hematologic abnormalities may be less frequent than with linezolid.[15]
Tigecycline (NF)	Consider **LFTs**[e] at baseline and every 2 weeks. **Coagulation tests** (i.e., aPTT, PTT, fibrinogen) at baseline and weekly during therapy.	Coagulopathy; GI upset (see comments); hepatotoxicity[f]; hypersensitivity, including anaphylaxis[d]; pancreatitis; photosensitivity; septic shock; treatment-related mortality (see comments)	Highly emetogenic - consider administration with anti-emetic. The cause of increased mortality risk seen during tigecycline trials is uncertain, but it is likely that most deaths were related to progression of patient's infection. Increased risk was most clearly seen in patients with ventilator-associated pneumonia.[16] Tigecycline has poor serum concentrations and should not be used for endovascular infections, including bacteremia.

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Vancomycin	**IV:** Inpatient, monitor **SCr/BUN** and urine output for potential nephrotoxicity as well as potential need for renal dose adjustment.[b] Check at baseline and then every 24-48 hours until stable vancomycin dosing is achieved. Recheck SCr every day after 3 days of vancomycin while inpatient. Outpatient, SCr/BUN should continue to be monitored twice weekly. Consider **CBCd** every 2 weeks for patients with prolonged use (> 14 days). Consider **clinical monitoring for hearing dysfunction** during treatment (at each clinic visit), particularly in those at risk for ototoxicity or those on prolonged therapy (>2 weeks). **Therapeutic drug monitoring:** For more information on timing of serum concentrations and goals refer to Vancomycin Guidelines in the **LPCHS HSM.** In outpatients, vancomycin troughs should be checked at least weekly, with more frequent monitoring indicated if signs of toxicity including renal function changes. **PO:** No routine laboratory monitoring. Consider clinical monitoring for symptoms of hypokalemia (e.g., fatigue, muscle weakness or spasms, constipation, palpitations) during treatment.	**IV:** Hematologic abnormalities (drug-induced immune thrombocytopenia, neutropenia); hypersensitivity, including anaphylaxis (rare)[d]; infusion-related reactions (see comments); nephrotoxicity[c]; ototoxicity (non-dose related, manifests as tinnitus, sensorineural hearing loss, dizziness, vertigo) **PO**: Dysgeusia; hypokalemia	Vancomycin per pharmacy protocol is preferred for inpatients at LPCHS (see policy). Monitor for vancomycin flushing syndrome; if a maculopapular rash appears on the face, neck, trunk, and/or upper extremities suggesting infusion reaction, refer to the LPCHS HSM for management recommendations.
Antimycobacterials Refer to Drug-Susceptible Tuberculosis Therapy Guideline for recommended monitoring and frequency related to treatment of tuberculosis.			
Ethambutol	Baseline **visual acuity** (Snellen test) and **color discrimination tests**, followed by monthly inquiry about visual disturbance and monthly color discrimination tests.	Dermatologic reactions; fever; ophthalmic (decreased visual acuity, red-green color blindness, optic neuritis)	
Isoniazid	**LFTs**[e] at baseline. If LFTs abnormal at baseline or in patients at increased risk for hepatotoxicity, consider repeat testing monthly.[h] For **pyrazinamide**, also measure **serum uric acid** at baseline and monthly during therapy.	Hepatotoxicity[f]; lupus-like syndrome; peripheral neuropathy	**Isoniazid:** Pyridoxine (vitamin B6) supplementation (1–2 mg/kg/day, max 50 mg/day) should be administered to malnourished patients, children or adolescents on meat or milk-deficient diets, breast-feeding infants, and those predisposed to neuritis to prevent peripheral neuropathy.
Pyrazinamide		Hepatotoxicity[f]; hyperuricemia; photosensitivity (rare)	
Rifampin	**LFTs**[e] and **CBC**. If LFTs abnormal at baseline or in patients at increased risk for hepatotoxicity, consider repeat testing monthly.[h] Repeat monthly monitoring of CBC only if abnormalities at baseline or based on clinical indication. **Coagulation tests** monthly in patients at risk of vitamin K deficiency (e.g., chronic liver diseases, poor nutritional status, prolonged use of antibacterial agents or anticoagulants).	Hematologic effects (hemolytic anemia, eosinophilia, thrombocytopenia); hepatotoxicity[f]; hypersensitivity reaction (immediate or flu-like syndrome); mental status changes	**Potential for drug-drug interactions**; known incompatibility of IV formulation with TPN. Counsel patients on change in color of body fluid to orange/red.
Rifapentine	**LFTs**[e] and **CBC** at baseline. If LFTs abnormal at baseline or in patients at increased risk for hepatotoxicity, consider repeat testing monthly.[h] Repeat monthly monitoring of CBC if abnormalities at baseline or based on clinical indication.	Hematologic effects (hemolytic anemia, eosinophilia, thrombocytopenia); hepatotoxicity[f]; hypersensitivity reaction;	Counsel patients on change in color of body fluid to orange/red.

Antimicrobial	Monitoring Frequency[a]	Common Potentially Serious ADRs (alphabetically)	Other Comments
Antifungals			
Amphotericin B deoxycholate (R)	Monitor **CBCd** and **LFTs**[e] weekly. Monitor **electrolytes (K and Mg [+ Ca, Na, and glucose for AmBisome®])** at baseline and twice weekly. Additional clinical monitoring for clinical symptoms of hypokalemia (muscle weakness, cramping, drowsiness, ECG changes, etc.) is also recommended. **SCr/BUN** twice weekly due to potential nephrotoxicity.[c] Monitor fluid status and input/output. Consider **ECG** prior to initiation if history of elevated QTc or on other potential QTc prolonging medication and repeat ECG 2-3 days after initiation of other QTc prolonging medication.	Electrolyte imbalance (hypokalemia, hypomagnesemia, [Ambisome only: hypocalcemia, hyponatremia, hyperglycemia]); hypersensitivity, including anaphylaxis[d]; infusion-related reactions (see comments); hematologic abnormalities (anemia; thrombocytopenia); hypotension; LFT abnormalities[f]; nephrotoxicity[c]; conditional risk of TdP[g]	Additional monitoring for signs and symptoms of infusion-related reactions (fever, shaking chills, hypotension, anorexia, nausea, vomiting, headache, tachypnea). Hydration is critical in reducing risk of nephrotoxicity – consider pre-hydration with a bolus of normal saline for each IV dose. For patients who are fluid sensitive, have pre-existing renal injury, or are unlikely to tolerate the fluid bolus, consider nephrology consult.
Amphotericin B (Liposomal) (AmBisome®) (R)			
Echinocandins			
Caspofungin	Consider monitoring **CBCd** and **LFTs**[e] at baseline and every 2 weeks for the first month, then monthly thereafter if on long-term therapy (>14 days). **Micafungin:** Isolated cases of significant renal dysfunction or acute renal failure have been reported. Routine SCr/BUN monitoring is not necessary, but should be considered if patients have signs indicating development of impaired renal function.[b]	Anemia; hepatotoxicity[f]; hypotension infusion-related reactions (see comments)	Isolated cases of possible histamine-related infusion reactions have occurred during trials (rash, flushing, pruritis, facial edema).
Micafungin (NF)		Acute renal failure; hematologic abnormalities (leukopenia, thrombocytopenia); hepatotoxicity[f]; infusion-related reactions (see comments)	
Azoles For more details on timing and therapeutic goals of **TDM** refer to *Azole Antifungal Therapeutic Drug Monitoring Guidance*			
Fluconazole	**LFTs**[e] at baseline and every 2 weeks for the first month, then monthly thereafter if on long-term therapy (>14 days). **SCr/BUN** at baseline and as needed for assessment of renal dose adjustment.[b] **TDM** not routinely recommended. Consider **ECG** prior to initiation if history of elevated QTc or on other potential QTc prolonging medication and repeat ECG 2-3 days after initiation of other QTc prolonging medication.	Hepatotoxicity[f]; known risk for TdP[g]	**Multiple potential drug-drug interactions** – notable medications including fentanyl, methadone, rifampin, sirolimus, tacrolimus, warfarin.
Itraconazole (NF)	Monthly **LFTs**[e] and **CBCd** in patients on prolonged therapy (>14 days). **TDM** recommended (refer to guideline). Consider **ECG** prior to initiation if history of elevated QTc, on other potential QTc prolonging medication, or unknown baseline QTc. For all except isavuconazole, repeat ECG 2-3 days after initiation of other QTc prolonging medication.	CNS depression; heart failure exacerbation; hepatotoxicity[f]; neuropathy; known risk TdP[g]	
Isavuconazole (R)	**LFTs**[e] at baseline and then monthly thereafter if on prolonged therapy (>14 days). Monitor **electrolytes (K)** at baseline and every 2 weeks. Additional clinical monitoring for symptoms of hypokalemia (muscle weakness, cramping, drowsiness, ECG changes, etc.) is recommended. **TDM** not routinely recommended.	Infusion-related reaction; hepatotoxicity[f]; hypokalemia	**Contraindicated** in patients with familial short QT syndrome; **multiple potential drug-drug interactions** (including fentanyl, rifampin, sirolimus, and tacrolimus).

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Posaconazole (R)	**CBCd, LFTs[e], and electrolytes (Ca, K, Mg)** at baseline and every 2 weeks for the first month, then monthly thereafter if on prolonged therapy (>14 days). **SCr/BUN** at baseline and as needed if concerned for renal impairment for assessment of renal dose adjustment (see comments).[b] **TDM** recommended (refer to guideline). Consider **ECG** prior to initiation if history of elevated QTc or on other potential QTc prolonging medication and repeat ECG 2-3 days after initiation of other QTc prolonging medication.	Electrolyte abnormalities (hypokalemia, hypomagnesemia, hypocalcemia); dermatological complications (e.g., rash); hematologic abnormalities (thrombocytopenia, leukopenia); hepatotoxicity[f]; known risk for TdP[g]	**Multiple potential drug-drug interactions** – notable medications including fentanyl, methadone, rifampin, sirolimus, tacrolimus, warfarin. **IV formulation** contains cyclodextrin vehicle which undergoes renal elimination and may accumulate in CrCl <50 ml/min. Cyclodextrins have been associated with kidney injury in animal models, but studies in humans have suggested similar rates of nephrotoxicity to noncyclodextrin-containing antifungals in patients with short durations. If IV used, monitor SCr periodically and switch to enteral therapy when clinically appropriate.[17] **Posaconazole:** Note that enteral formulations not interchangeable.
Voriconazole	**LFTs[e] and electrolytes (K, Mg)** at baseline and every 2 weeks for the first month, then monthly thereafter if on long-term therapy (>14 days). **SCr/BUN** at baseline and as needed if concerned for renal impairment for assessment of renal dose adjustment (see comments).[b] **TDM** recommended (refer to guideline). Consider **ECG** prior to initiation if history of elevated QTc or on other potential QTc prolonging medication and repeat ECG 2-3 days after initiation of other QTc prolonging medication.	Electrolyte abnormalities (hyper/hypokalemia, hypomagnesemia); dermatological complications (e.g., cutaneous malignancies); hepatotoxicity[f]; hypersensitivity, delayed (e.g., SJS, TEN); ocular and neurological effects (e.g., visual disturbances, optic neuritis, vision color changes, scleritis, peripheral neuropathy, encephalopathy); periostitis; photosensitivity; known risk for TdP[g]	
Antivirals			
Acyclovir	**IV:** Monitor **CBCd** and **LFTs[e]** weekly in infants and children. Neonates receiving acyclovir 60 mg/kg/DAY IV should have neutrophil count monitoring at least twice weekly. **SCr/BUN** weekly due to potential nephrotoxicity as well as potential need for renal dose adjustment.[b] **PO: CBCd** including absolute neutrophil count should be assessed at 2 and 4 weeks after initiating and then monthly during long-term therapy.	Crystalluria leading to acute renal injury[c]; hypersensitivity, delayed (rare, i.e., SJS/ TEN); hematologic abnormalities (neutropenia, thrombocytopenia); LFT abnormalities[f]; neurotoxicity (e.g., confusion, agitation, hallucination, and seizure); thrombotic microangiopathy	Hydration is critical in reducing risk of nephrotoxicity – consider pre-hydration with a bolus of normal saline for each IV acyclovir dose. For patients who are fluid sensitive, have pre-existing renal injury, or are unlikely to tolerate the fluid bolus, consider nephrology consult.
Cidofovir (R)	Monitor **CBCd** at baseline and prior to each dose. **SCr/BUN** and **urine protein** should be assessed at baseline and within 48 hours of each dose for nephrotoxicity monitoring and potential renal dose adjustment.[b] Monitor hydration status before, during, and after infusion. **LFTs[e]** and **electrolytes (bicarbonate**) weekly. **Weekly urinalysis** and **uric acid**. Check **intraocular pressure** and **visual acuity** at baseline and as needed for patient complaints of eye pain, vision loss/distortion, or clinical signs of iritis/uveitis.	**Carcinogenic/teratogenic**; hematologic abnormalities (anemia; neutropenia); LFT abnormalities[f]; metabolic acidosis; nephrotoxicity[c]; ocular complications (iritis, uveitis, decreased intraocular pressure); rash	Hydration is critical in reducing risk of nephrotoxicity – Hydrate with normal saline before/ during/ after each dose +/- probenecid (refer to HSM for details). For patients who are fluid sensitive, have pre-existing renal injury, or are unlikely to tolerate the fluid bolus, consider nephrology consult.

Antimicrobial	Monitoring Frequency[a]	Common Potentially Serious ADRs (alphabetically)	Other Comments
Foscarnet (R)	During induction therapy: obtain **CBCd** and **electrolytes (including Ca, Mg, K, and phosphorus**) twice weekly and then once weekly during maintenance therapy. More frequent monitoring may be required in some patients. **SCr/BUN** should be assessed at baseline and then two to three times weekly for nephrotoxicity monitoring and potential renal dose adjustment.[b] Monitor hydration status before and after infusion. Consider **ECG** prior to initiation if history of elevated QTc or on other potential QTc prolonging medication and repeat ECG 2-3 days after initiation of other QTc prolonging medication.	Electrolyte disturbances (hypokalemia, hypocalcemia, hypomagnesemia, hypophosphatemia); genital vascular tissue damage and ulceration; hematologic abnormalities (anemia; granulocytopenia); nephrotoxicity[c] neurotoxicity (i.e., seizure); conditional risk for TdP[g]	Hydration is critical in reducing risk of nephrotoxicity – Hydrate with NS or D5W prior to the first dose. Additional hydration is recommended with each dose. For patients who are fluid sensitive, have pre-existing renal injury, or are unlikely to tolerate the fluid bolus, consider nephrology consult.
Ganciclovir	Monitor **CBCd** at baseline then once to twice weekly. Consider twice weekly monitoring especially in patients with renal impairment, neutrophil count <1000 cells/mm^3 at initiation, or history of drug-induced leukopenia. **SCr/BUN** weekly due to potential nephrotoxicity as well as potential need for renal dose adjustment.[b]	**Carcinogenic**; fetal toxicity and impairment of fertility; fever; hematologic abnormalities (granulocytopenia, leukopenia, anemia, thrombocytopenia, pancytopenia); nephrotoxicity[c]	Concurrent use with imipenem-cilastatin is **not** recommended due to increased risk of breakthrough seizure.
Letermovir (R)	No routine laboratory monitoring. Consider at least monthly **CBCd** in patients on prolonged therapy (> 28 days).	Cough; GI side effects; thrombocytopenia	
Remdesivir (R)	Consider **LFTs**[e] and **prothrombin time** at baseline and at 3 days of therapy (for 5-day course) for inpatients or when clinically indicated for outpatients.	Bradycardia and hypotension; hypersensitivity, including anaphylaxis[d]; infusion-related reactions; hepatotoxicity[f]	
Valacyclovir	**CBCd**, specifically absolute neutrophil count, should be assessed at 2 and 4 weeks after initiating long-term therapy and then monthly during therapy. Routine **SCr/BUN** monitoring is not necessary but should be considered if patients have signs indicating development of impaired renal function.[b]	Nephrotoxicity[c]; neutropenia; neurotoxicity (agitation, confusion, hallucination, ataxia, tremor, seizure); thrombotic microangiopathy	
Valganciclovir	**Absolute neutrophil counts** should be performed weekly for 6 weeks, then at 8 weeks, then monthly for the duration of antiviral use; **LFTs**[e] should be measured monthly during use.	**Carcinogenic/teratogenic**; hematologic abnormalities (leukopenia, thrombocytopenia)	Concurrent use with imipenem-cilastatin is **not** recommended due to increased risk of breakthrough seizure.

Abbreviations: ADR, adverse drug reaction; ALT, alanine transaminase; AST, aspartate transaminase; BUN, blood urea nitrogen; Ca, calcium; CBA, colistin base activity; CBCd, complete blood count with differential; CF, cystic fibrosis; CK, creatinine kinase; CNS, central nervous system; D5W, 5% dextrose in water; DRESS, drug reaction with eosinophilia and systemic symptoms; ECG, electrocardiogram; GI, gastrointestinal; HSM, LPCHS Housestaff Manual; INR, international normalized ratio; K, potassium; LFT, liver enzyme function test; Mg, magnesium; Na, sodium; (NF), non-formulary restricted antimicrobial during hospitalization where use requires approval by Pediatric Infectious Diseases; NS, normal saline; PO, by mouth; PT, prothrombin time; QTc, corrected QT interval; (R), restricted antimicrobial during hospitalization where use requires approval by Pediatric Infectious Diseases; SCr, serum creatinine; SJS, Steven-Johnson Syndrome; SMX, sulfamethoxazole; TDM, therapeutic drug monitoring; TdP, Torsades de Pointes; TEN, toxic epidermal necrolysis; TMP, trimethoprim

a. These recommendations are based on frequency and seriousness of reported adverse events. The monitoring plan for an individual patient may be different based on the comorbid conditions and anticipated duration, especially in prolonged outpatient therapy. For instance, for shorter courses of linezolid, ceftriaxone, or clindamycin, it may not be necessary to monitor LFTs and/or

renal function. Alternatively, for longer courses of fluoroquinolones, weekly lab monitoring may be appropriate. For patients with normal baseline labs, less intense monitoring may be appropriate. For rifampin, consider baseline LFTs, SCr, and CBC, with periodic monitoring (every 2 to 4 weeks) based on patients baseline abnormalities.

b. For dose adjustment recommendations, refer to the LPCH Antimicrobial Renal Dose Adjustment Guideline. Inpatients who are considered exposed to a high nephrotoxin burden per NINJA protocol should have SCr monitored daily.
c. Refer to KDIGO guidelines for clinical definition and diagnosis of acute kidney injury.
d. Anaphylaxis is characterized by urticaria, angioedema, rhinitis, bronchospasm, and anaphylactic shock occurring within the first hour after drug administration. Patients should be monitored for signs of anaphylaxis during first dose.
e. Liver enzyme function tests (include ALT, AST, alkaline phosphatase, albumin, and total bilirubin).
f. Drug induced liver injury (DILI) is a diagnosis of exclusion and relies upon assessment of time to onset of hepatotoxicity, risk factors, exclusion of alternative non-drug-related causes of acute liver injury, and establishment of a possible causal association between a drug and liver injury. Patients thought to be experiencing drug-associated hepatotoxicity should be evaluated for drug discontinuation and supportive care. Refer to LiverTox for more information on DILI for specific medications.
g. Risk of Torsades de Pointes (TdP): 'Known risk' means the medication is known to prolong QTc interval and cause TdP, even when taken as recommended; 'possible risk' means can cause QTc prolongation but not known to cause TdP when taken as recommended; 'conditional' means associated with TdP but only under certain conditions (e.g., excessive dose, with hypokalemia, with other interacting drugs) or by creating conditions that induce TdP (inhibiting metabolism of QTc prolonging drugs); Source for TdP risk (CredibleMeds.org)
h. Factors that may increase patients' risk for hepatotoxicity include: abnormal LFTs at baseline, symptoms consistent with hepatotoxicity (e.g., rash, stomach pain, nausea and vomiting, fatigue, dark-colored urine, light-colored bowel movements, jaundice, loss of appetite, and/or fever), patients who take other potentially hepatotoxic medications or have viral hepatitis or history of liver disease, HIV, or prior drug-induced liver injury.

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