# Antimicrobial Guidebook – 2025 Edition



#### **Prepared by:**

Theora Canonica, Pharm.D. Clara Lee, Pharm.D., BCPS Jennifer Mulliken, M.D. Mai Vu, Pharm.D.

#### Approved by:

Antimicrobial Stewardship Committee Pharmacy and Therapeutics Committee Infectious Diseases Section

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## **ID/ASP Contact Information**

ASP/ID Pharmacist Sunday - Wednesday ASP/ID Pharmacist Wednesday - Saturday ID Fellow HIV Pharmacist Outpatient Pharmacy Inpatient Pharmacy Microbiology Lab Lab Send Out Infection Control (6AM – 4:30PM) Occupational Health (8AM – 4:30PM) Pager (415) 223 – 8046 or EXT 25269 Pager (415) 223 – 8046 or EXT 23763 Pager (415) 443 – 5151 EXT 24793 EXT 22708 EXT 22934 or 22935 EXT 22267 or 23782 EXT 26583 EXT 26583 EXT 26269 Phone (415) 469 – 4411

### **ID Resources**

SFVA Specific Guidelines on SFVA Intranet

- Isolation Instructions (type of isolation by organism), interpreting C. Diff testing results, rule out TB algorithm:
   <u>Infection Control Algorithms All Documents (sharepoint.com)</u>
- SFVAMC Antibiogram:
  - SFVAMC SharePoint: Antibiograms
- Infection Control Manual:
  - o Infection Control IC Manual All Documents (sharepoint.com)
- UCSF Infectious Diseases Management Program:
  - Guidelines for Empiric Antimicrobial Therapy
    - o <u>https://idmp.ucsf.edu/guidelines-empiric-antimicrobial-therapy</u>
  - Antimicrobial Dosing Guidelines
    - o <u>https://idmp.ucsf.edu/antimicrobial-dosing-guidelines</u>

SFVA Specific Guidelines under Hospital Specific Guidelines on IDMP:

- VASF Antimicrobial Guidebook
  - o <u>Guidelines At VASF | Infectious Diseases Management Program at UCSF</u>

## **ID Restricted Antimicrobial Prior Authorization Process**

Several <u>formulary antimicrobial medications</u> are locally restricted to specialty services such as infectious diseases (ID) as part of ongoing antimicrobial stewardship measures to reduce collateral effects such as the emergence of antimicrobial resistance, *C. difficle* infection, and drug associated toxicities.

Antimicrobials restricted to the ID service are available to order by house staff BUT require prior approval by ID provider/ ASP pharmacist before processing pharmacist will release the medication order. If an order for an ID restricted agent is received without prior approval, pharmacist will make a reasonable attempt to contact prescribing provider/ ordering service.

#### ID/ASP Antimicrobial Approval Coverage:

- Monday Sunday 8 am to 6:30 pm → Contact ASP Pharmacist (pager: 223-8046 or EXT 25269 or 23763)
- Monday Sunday 6:30 pm to 10 pm & Holidays → Contact ID Fellow (pager: 415-443-5151)

Restricted agents ordered during off hours will be processed as one-time doses by pharmacy and reviewed for continuation by ID/ASP during business hours. Restricted antimicrobials may be continued when patients transfer units including antimicrobials initiated in the ICU prior to transfer.

## **Available Antimicrobials at SFVA**

#### Shaded = Restricted to Infectious Diseases (ID) service \* = Restricted to indication and/or non-ID specialty service NFDR=Pharmacy NFDR Consult required

ANTIBIOTICS
AMIKACIN LIPOSOME 590MG/8.4ML INHL SUSP NFDR
AMIKACIN SULFATE 250MG/ML INJ
AMOXICILLIN 125MG SUSP, 250MG CAP/SUSP, 500MG CAP
AMOXICILLIN/CLAV 500/125MG, 875/125MG TAB
AMOXICILLIN/CLAV 400/ 57MG / 5 ML PO SUSP
AMPICILLIN 500MG INJ/PO*, 1GM INJ, 2GM INJ *Consult Rx
AMPICILLIN /SULBACTAM 1.5GM INJ, 3GM INJ
AZITHROMYCIN 250MG TAB/SUSP, 600MG TAB; 500MG INJ
AZTREONAM 1GM, 2GM INJ*SEVERE PENICILLIN-ALLERGY,
OTHER USES NEED ID APPROVAL
CEFACLOR 250MG, 500MG CAP
CEFADROXIL 500MG CAP
CEFAZOLIN 1GM, 2GM INJ*ID IF DOSE > Q 8H
CEFDINIR 300MG CAP
CEFEPIME 1GM, 2GM INJ * <i>ICU, ED, HEM/ONC; PERI-OP</i>
NEUROSURG
CEFIDEROCOL 1GM INJ
CEFOXITIN 1GM INJ
CEFPODOXIME PROXETIL 100MG, 200MG TAB
CEFTAROLINE FOSAMIL 600MG INJ
CEFTAZIDIME 1GM; 2GM INJ
CEFTAZIDIME/AVIBACTAM 2.5GM INJ
CEFTOLOZANE/TAZOBACTAM 1.5GM INJ
CEFTRIAXONE 250MG, 2GM, 1GM INJ
CEFUROXIME 0.75GM, 1.5GM INJ* OPHTHAMOLOGY
CEPHALEXIN 250MG, 500MG CAP; 250 MG/5ML SUSP NFDR
CHLORAMPHENICOL 1GM INJ
CIPROFLOXACIN 250MG, 500MG, 750MG TAB; 200MG,
400MG INJ* GI, x1 PRE-OP (restrictions for inpatient ONLY)
CIPROFLOXACIN 500MG/5ML SUSP <sup>NFDR*</sup> GI (restrictions for
inpatient use ONLY) CLARITHROMYCIN 250 MG (IP use); 500MG TAB
CLARITHROMYCIN 125 MG/ 5ML, 250MG/5ML SUSP <sup>NFDR</sup>
CLINDAMYCIN HCL 150MG CAP* ORAL SURG & ENT (service
restrictions for Inpatient use ONLY)
CLINDAMYCIN 75MG/5ML ORAL SOLN *ORAL SURG & ENT
(service restrictions for Inpatient use ONLY)
CLINDAMYCIN PHOS 600MG; 900MG INJ
COLISTIMETHATE (COLISTIN BASE 150MG) INJ <sup>NFDR</sup>
DALBAVANCIN 500 MG INJ NFDR
DELAFLOXACIN 450 MG TAB NFDR
DICLOXACILLIN 250MG CAP
DOXYCYCLINE 20MG TAB*, 50MG TAB, 100MG TAB & INJ
*VA DENTAL and DERM ONLY
DURLOBACTAM/SULBACTAM 1/1GM INJ
ERAVACYCLINE 50MG INJ
ERTAPENEM 500MG, 1GM INJ
ERYTHROMYCIN BASE 250MG TAB* COLORECTAL SX PPX
ERYTHROMYCIN ES 400MG/5ML PO SUSP; 500MG, 1GM INJ
FIDAXOMICIN 200MG TAB *orderable via CDI order menus

FOSFOMYCIN TROMETHAMINE 3GM SACHET <sup>NFDR</sup>
GENTAMICIN 10MG, 40 MG INJ
IMIPENEM-CILASTATIN 500MG INJ
IMIPEN/RELEBACT-CILASTATIN 1.25GM INJ
LEVOFLOXACIN 250MG, 500MG, 750MG TAB & INJ*
HEM/ONC EXCEPT FOR PENICILLIN-ALLERGIC PTS W/ CAP
LINEZOLID 600MG TAB & INJ; 100MG/5ML SUSP,ORAL
MEROPENEM 500MG, 1GM, 2GM INJ
METRONIDAZOLE 250MG, 500MG TAB; 500MG INJ
MINOCYCLINE HCL 50MG, 100MG CAP* DERM
MINOCYCLINE HCL 100MG/VIL INJ <sup>NFDR</sup>
MOXIFLOXACIN HCL 400MG TAB
MUPIROCIN 2% OINT
NAFCILLIN 1GM, 2GM INJ
NEOMYCIN SULFATE 500MG TAB
NITROFURANTOIN MONO/MACRO 100MG CAP
NORFLOXACIN 400MG TAB <sup>NFDR</sup>
OFLOXACIN 200MG, 300MG, 400MG TAB <sup>NFDR</sup>
PENICILLIN G BENZATHINE 1.2MU/2ML INJ
PENICILLIN G POTASSIUM 20 MU INJ
PENICILLIN G PROCAINE 1.2 MU TUBEX
PENICILLIN G SODIUM 5 MU INJ <sup>NFDR</sup>
PENICILLIN VK 250MG, 500MG TAB
PENICILLIN VK 250MG/5ML SOLN
PIPERACILLIN TAZOBACTAM 2.25GM, 3.375GM, 4.5GM
INJ*ICU, ED OR SINGLE PERI-PROCEDURAL DOSES
POLYMYXIN-B 500,000U INJ
RIFAXIMIN 550MG TAB <sup>NFDR</sup>
STREPTOMYCIN 1GM INJ
SULFAMETHOX/TMP 80/16MG/ML INJ
SULFAMETHOX/TMP 200/40MG/5ML SUSP
SULFAMETHOX/TMP 200/20100/SME 303P
TEDIZOLID 200 MG TAB <sup>NEDR</sup>
TETRACYCLINE 250MG*, 500MG CAP* H. Pylori Treatment
TIGECYCLINE 50MG INJ
TRIMETHOPRIM 100MG TAB
TOBRAMYCIN SULFATE 40MG INJ; 300MG/5 ML PO SOLN <sup>NFDR</sup>
VANCOMYCIN SOLFATE 4000G INJ; SOUNG/S ME PO SOLINUSA VANCOMYCIN HCL 125MG CAP* Outpatient restriction: NEED
ID OK if dose exceeds 125MG QID X 10 days VANCOMYCIN HCL 1GM INJ
VANCOMYCIN HCL 25MG/ML ORAL SOLN
ANTIFUNGALS
AMPHOTERICIN B CONVENTIONAL 50MG INJ
AMPHOTERICIN B LIPOSOME 50MG INJ
FLUCONAZOLE 50MG, 100MG, 150MG, 200MG TAB
FLUCONAZOLE 10MG/ML 40MG/ML PO SUSP
FLUCONAZOLE 200MG; 400MG INJ
FLUCYTOSINE 250MG, 500MG CAP
ISAVUCONAZONIUM SULFATE 186MG ORAL CAPNEDR
ISAVUCONAZONIUM SULFATE 372MG INJ <sup>NEDR</sup>
ITRACONAZOLE 100MG CAP & 50MG/5ML ORAL SOLN
KETOCONAZOLE 200MG TAB* HEM/ONC, ENDO
MICAFUNGIN 50MG; 100MG INJ
POSACONAZOLE 100MG EC TAB* HEM/ONC
TERBINAFINE 250MG TAB
VORICONAZOLE, 50MG, 200MG TAB & 200MG INJ
VORICONAZOLE 200MG/5ML ORAL SUSP <sup>NEDR</sup>

ANTIVIRALS
ACYCLOVIR 200MG CAP, 400MG TAB, 800MG TAB
ACYCLOVIR 200 MG/ 5 ML ORAL SUSP <sup>NFDR</sup>
ACYCLOVIR 500MG, 1GM INJ
ADEFOVIR DIPIVOXIL 10MG TAB* LIVER
CIDOFOVIR 75MG/ML INJ
EMTRICITABINE 200MG/TAF 25MG TAB* for HIV PREP
EMTRICITABINE 200MG/TDF 300MG TAB* for HIV PREP
ENTECAVIR 0.5MG, 1MG TAB* LIVER, RHEUM, HEM/ONC
FAMCICLOVIR 125MG, 250MG, 500MG TAB* DERM
GANCICLOVIR 500MG CAP <sup>NFDR</sup> & 500MG INJ
LAMIVUDINE 100MG, 150MG, 300MG TAB *Liver
LAMIVUDINE 50MG/5ML ORAL SOLN* Liver
LETERMOVIR 480 MG <sup>NFDR</sup> *HEM/ONC
OSELTAMIVIR 30MG, 75MG CAP
OSELTAMIVIR 6MG/ML ORAL SUSP <sup>NFDR</sup>
REMDESIVIR 100MG INJ* Use > 5 days Requires ID Approval
TENOFOVIR ALAFENAMIDE (TAF) 25MG TAB* Liver
TENOFOVIR DISOPROXIL FUMARATE (TDF) 300MG TAB* LIVER
VALACYCLOVIR HCL 500 MG, 1GM TAB
VALGANCICLOVIR HCL 450MG TAB
ZANAMIVIR 5MG INHL
COVID-19
BARICITINIB 1MG, 2MG TAB <sup>NFDR</sup>
INV-MOLNUPIRAVIR 200MG ORAL CAP* EUA criteria for use
PAXLOVID = GOV-NIRMATRELVIR 150 MG TAB + GOV-
RITONAVIR 100 MG TAB* Use > 5 days Requires ID Approval
REMDESIVIR 100MG INJ* Use > 5 days Requires ID Approval
TOCILIZUMAB 20 MG/ML INJ <sup>NFDR</sup>
MISCELLANEOUS ANTI-INFECTIVES
ALBENDAZOLE 200MG TAB
ATOVAQUONE 750MG/5ML ORAL SUSP
ATOVAQUONE 250MG/PROGUANIL HCL 100MG TAB
DAPSONE 25MG, 100MG TAB
CYCLOSERINE 250MG CAP
ETHAMBUTOL HCL 100MG, 400MG TAB
ETHIONAMIDE 250MG TAB
HYDROXYCHLOROQUINE 100MG, 200MG TAB*DERM, RHEUM
ISONIAZID 100MG, 300MG TAB & 50MG/5ML SYRUP <sup>NFDR</sup>
IVERMECTIN 3MG TAB <sup>NFDR*</sup> DERM
LACTOBACILLUS ACIDOPHILUS TAB
MEFLOQUIN 250MG TAB <sup>NFDR</sup>
NITAZOXANIDE 500MG TAB <sup>NFDR</sup>
PAROMOMYCIN SULFATE 250MG CAP <sup>NFDR</sup>
PEGINTERFERON ALFA-2A 180MCG/ML INJ* LIVER CLINIC
PENTAMIDINE ISETHIONATE 300MG/VI INJ
PRIMAQUINE PHOSPHATE 26.3MG TAB
PYRAZINAMIDE 500MG TAB
QUININE SULFATE 324MG CAP <sup>NFDR</sup>
RIFABUTIN 150MG CAP
RIFAMPIN 150MG, 300MG CAP
RIFAMPIN 600MG INJ*ONE-TIME FOR O.R. GRAFT SOAKING
RIFAPENTINE 150MG TAB *VA LTBI CLINIC ONLY
SULFADIAZINE 500MG TAB
TINIDAZOLE 500MG TAB <sup>NFDR</sup>

## Antibiograms (Non-Urine and Urine)

#### Please note the following comments:

- All data is reported as percent fully susceptible
- First isolate per patient per organism is counted in the antibiogram
- 30 organisms are required to report susceptibilities on an antibiogram per CLSI guidelines. Some organisms were included in despite less than 30 organisms isolated
- When treating UTIs caused by *E. Coli, Klebsiella spp.*, and *Proteus spp.*, cefazolin can be used to predict results for the following oral agents: cephalexin (Keflex) and cefpodoxime (Vantin)
- Gentamicin susceptibilities for *enterococcus spp.* are for gram-positive synergy
- <u>Non-urine</u> coagulase-negative staphylococcus includes: S. auricularis, S. capitis, S. haemolyticus, S. hominis, S. lugdunensis, S. simulans, S. ureilyticus, S. warneri
- <u>Urine</u> coagulase-negative staphylococcus includes: S. epidermidis, S. haemolyticus, S. lugdunensis, and S. warneri
- Key: ESBL: Extended-spectrum beta-lactamase; CR: Carbapenem resistant; VRE: Vancomycin resistant enterococci; MR: Methicillin resistant; NA: Not available; R: Intrinsically resistant

	# Isolates	Ampicillin	Cefazolin	Ceftriaxone	Ertapenem	Piperacillin/ tazobactam	Cefepime	Ciprofloxacin	Levofloxacin	Gentamicin	Oxacillin	Sulfamethoxazole/ trimethoprim	Clindamycin	Doxycycline	Vancomycin	Linezolid	Daptomycin
Gram negative																	
Escherichia coli (ESBL 12%)	67	55	NA	81	100	94	81	70	69	90	R	NA	R	R	R	R	R
Klebsiella pneumoniae (ESBL 19%)	27	R	NA	89	100	96	89	89	85	100	R	NA	R	R	R	R	R
Proteus mirabilis	26	73	NA	73	100	100	73	69	86	95	R	73	R	R	R	R	R
Pseudomonas aeruginosa (CR 11%)	44	R	R	R	R	88	93	84	79	R	R	R	R	R	R	R	R
Gram positive																	
Enterococcus faecalis	72	100	R	R	R	100	R	NA	NA	82	NA	R	R	NA	99	100	100
Staphylococcus aureus	228	R	70	NA	NA	NA	NA	NA	NA	R	70	94	79	96	100	100	100
MSSA (70%)	159	R	100	NA	NA	NA	NA	NA	NA	R	100	97	81	96	100	100	100
MRSA (30%)	69	R	R	NA	NA	NA	NA	NA	NA	R	R	87	74	97	100	100	100
Coagulase-negative staph (MR 52%)	83	R	48	NA	NA	NA	NA	NA	NA	R	48	68	59	86	99	100	100
Staphylococcus epidermitis (MR 44%)	34	R	56	NA	NA	NA	NA	NA	NA	R	56	57	57	83	98	100	100

#### **Non-Urine Culture Antibiogram**

#### **Urine Culture Antibiogram**

	# Isolates	Amoxicillin/ clavulanate	Ampicillin	Cefazolin	Cefepime	Ceftriaxone	Ciprofloxacin	Ertapenem	Levofloxacin	Nitrofurantoin	Sulfamethoxazole /trimethoprim	Oxacillin	Vancomycin
Gram negative													
Enterobacter cloacae complex	45	R	R	R	96	R	89	96	89	60	87	R	R
Escherichia coli (ESBL 15%)	442	83	45	81	84	84	70	100	64	99	69	R	R
Klebsiella oxytoca (ESBL 7%)	30	97	R	90	93	90	100	100	100	87	97	R	R
Klebsiella pneumoniae (ESBL 13%)	142	94	R	85	86	85	84	100	80	49	79	R	R
Proteus mirabilis (CR 1%)	89	88	73	73	74	73	72	99	71	R	64	R	R
Pseudomonas aeruginosa (CR 15%)	67	R	R	R	82	R	83	R	73	R	R	R	R
Gram positive													
Enterococcus faecalis (VRE 0%)	108	100	100	R	R	R	R	R	NA	100	R	NA	100
Staphylococcus aureus (MRSA 39%)	44	NA	R	61	NA	NA	R	R	NA	100	84	61	100
Coagulase-negative staphylococcus	201	NA	R	54	NA	NA	R	R	NA	99	69	54	100

## **Spontaneous Bacterial Peritonitis (SBP)**

Approximately 1/3 of cirrhotic patients have bacterial infections. Spontaneous bacterial peritonitis (SBP) is a common infection in this setting which occurs in the absence of an obvious source of infection. Presence of fever or hypothermia, chills, and localizing symptoms should raise suspicion for bacterial infection. Signs/symptoms specific to SBP are abdominal pain, tenderness on palpation +/- rebound tenderness, and ileus. However, typical symptoms may be absent in cirrhotic patients. Common pathogens include gut bacteria (*E. coli, Klebsiella spp.*) and *Streptococci spp*.

#### **Diagnosis**

- Diagnostic abdominal paracentesis for cell count and bacterial culture, even in absence of signs/symptoms of infection.
   Culture ascitic fluid <u>before</u> initiating antibiotics.
- Polymorphonuclear (PMN) leukocyte count >250/mm<sup>3</sup> indicates SBP → Start empiric antibiotics.

#### I. <u>SBP Empiric Treatment:</u> Expected duration 5-7 days

SBP Infection	Empiric Therapy					
Community Acquired <sup>+</sup>	Ceftriaxone 1 gm IV q24h					
Nosocomial**	Piperacillin/tazobactam^* 4.5 gm IV q6h					
Septic shock; History of ampicillin-resistant <i>enterococcus</i> infection; IV antibiotic use and hospitalization within prior 90 days; Positive MRSA nasal swab or prior MRSA infection	Piperacillin/tazobactam^* 4.5 gm IV q6h <b>PLUS</b> Vancomycin IV ( <u>see pages 44-45 for dosing</u> )					
History of Vancomycin-Resistant Enterococcus spp. (VRE)	Piperacillin/tazobactam^* 4.5 gm IV q6h PLUS Daptomycin* 10 mg/kg IV q24h					

\* Present at or acquired within the first 48 hours of admission \*\* Acquisition of infection >48 hours after admission

^ If patient received > 48 hours of piperacillin/tazobactam within the prior 60 days, consider empiric meropenem\*

\* Contact ASP PharmD (preferred) or ID fellow for approval (EXCEPTION: pip/tazo may be used in ICU without ID prior approval)

#### II. SBP Prophylaxis

Prophylaxis Criteria	Antibiotic Therapy	Duration	
Primary Prophylaxis	Preferred: Ceftriaxone 1 gm IV Q24H	7 days	
Advanced cirrhosis <u>without</u> prior episode of SBP <u>and</u> Acute upper gastrointestinal hemorrhage	Alterative initial agent/ PO step down: Ciprofloxacin* 500 mg PO q12h Sulfamethoxazole-trimethoprim 1 DS PO tab q12h		
Primary Prophylaxis         Low ascitic protein (<1.5 g/dL) AND	Preferred: Ciprofloxacin* 500 mg PO Q24H Alternative: Sulfamethoxazole-trimethoprim 1 DS PO tab daily	Long term	
<u>Secondary Prophylaxis</u> Prior episode of SBP	Preferred: Ciprofloxacin* 500 mg PO Q24H Alternatives: Sulfamethoxazole-trimethoprim 1 DS PO tab daily Rifaximin# 400 mg PO TID (preferred) or 550 mg PO BID	Long term	

\* Place pharmacy NFDR consult \* Contact ASP PharmD (preferred) or ID fellow for inpatient use

References: 1. Biggins, Scott W., et al. "Diagnosis, evaluation, and management of ascites, spontaneous bacterial peritonitis and hepatorenal syndrome: 2021 practice guidance by the American Association for the Study of Liver Diseases." Hepatology 74.2 (2021): 1014-1048.

# **Urinary Tract Infections (UTI)**

#### <u>Diagnosis</u>



Pyuria, cloudy urine, foul smell, or positive urinalysis are NOT symptoms of urinary tract infection (UTI) and are NOT indications for antibiotic therapy



#### **Common Causative Organisms**

E. coli, Proteus spp., Klebsiella spp. Pseudomonas spp. (if at least 1 risk factor^ present)

^<u>Pseudomonal risk factors</u> include: hospitalization within the last 30 days AND received IV antibiotics, history of prior pseudomonal infection, immunocompromised (uncontrolled HIV, transplant, etc.)

#### **Uncomplicated vs complicated UTI**

- Uncomplicated: UTI in a patient with a normal GU tract and no recent instrumentation
- Complicated: UTI in the presence of an <u>anatomic abnormality</u>, <u>functional abnormality</u>, <u>recent GU instrumentation</u>, <u>or foreign material (e.g., ureteral stent)</u>

#### **Clinical Pearls**

- When results are available, treatment should be tailored based on culture data
  - Asymptomatic bacteriuria does not require antibiotic therapy for most patients. Antibiotics are only indicated for: • Pregnancy: cystitis treatment
    - Urological procedure: 1 dose prior to procedure and 1 to 2 doses after
- Catheter associated UTIs (CAUTI) require change in catheter and then may be treated based on site of infection
- Lower cefepime doses are used to treat Pseudomonal UTIs compared to systemic pseudomonal infections due to high urinary concentration (85% of unchanged drug excreted via urine)

#### Empiric Outpatient UTI Treatment (CPRS Ambulatory Care Order Menu Available)

Diagnosis	Preferred Treatment	Duration		
Linconneliested	Cephalexin 500 mg PO q12h	7 days		
Uncomplicated cystitis	Nitrofurantoin 100 mg PO q12h	Male: 7 days <u>Female</u> : 5 days		
Cystitis	Ciprofloxacin 500 mg PO q12h (pseudomonas risk^)	7 days		
	Cefpodoxime 200 mg PO q12h	Prompt symptom resolution: 7		
CAUTI	Sulfamethoxazole-trimethoprim 1 DS PO q12h	days		
	Ciprofloxacin 500 mg PO q12h (pseudomonas risk^)	Delayed response: 10 - 14 days		
	Ceftriaxone 1 gm x1 IM, then Cefpodoxime 200 mg PO q12h	10 – 14 days		
Pyelonephritis or	Sulfamethoxazole-trimethoprim 1 DS PO q12h	10 - 14 days		
complicated UTI	Ciprofloxacin 500 mg PO q12h (pseudomonas risk^)	7 days		
	Levofloxacin* 500 mg PO daily			
Epididymitis	If concerned about sexually transmitted chlamydia and gonorrhea <u>ADD</u> : Doxycycline 100 mg PO BID x7 days <u>AND</u> one-time dose of IM ceftriaxone: Total body weight < 150 kg: ceftriaxone 500 mg IM x1 Total body weight ≥ 150 kg: ceftriaxone 1000 mg IM x1	10 days		
Acute bacterial	Sulfamethoxazole-trimethoprim 1 DS PO q12h	14 days		
prostatitis	Ciprofloxacin 500 mg PO q12h			
Chronic prostatitis	Consider consulting urology service			

#### **Empiric Inpatient UTI Treatment**

Diagnosis	Preferred Treatment	Duration
Community acquired	Cephalexin 500 mg PO q12h	7 days
Community acquired uncomplicated cystitis	Nitrofurantoin 100 mg PO q12h	Male: 7 days <u>Female</u> : 5 days
uncomplicated cystitis	Ciprofloxacin* 500 mg PO q12h ( <i>pseudomonas</i> risk^)	7 days
	Ceftriaxone 1 gm IV q24h	All IV or step down to PO
Community acquired	Cefepime* 2 gm IV q12h ( <i>pseudomonas</i> risk^)	fluroquinolone: 7 days
pyelonephritis or		
complicated UTI		PO Step down to beta-lactam or
		sulfa-trimethoprim: 10 - 14 days
Healthcare associated	Ertapenem 1 gm IV q24h	Brompt symptom resolution: 7 days
complicated or	Cefepime* 2 gm IV q12h (pseudomonas risk^)	Prompt symptom resolution: 7 days Delayed response: 10 - 14 days
uncomplicated UTI		Delayeu l'esponse. 10 - 14 days
CALITI	Ceftriaxone 1 gm IV q24h	Prompt symptom resolution: 7 days
CAUTI	Cefepime* 2 gm IV q12h (pseudomonas risk^)	Delayed response: 10 - 14 days
Acute bacterial Sulfamethoxazole-trimethoprim 1 DS PO q12h		14 days
Prostatitis	Ciprofloxacin* 500 mg PO q12h	14 days

\*Contact ASP Pharmacist (preferred) or ID fellow to approve use outside of ICU

^<u>Pseudomonal risk factors</u> include hospitalization within the last 30 days AND received IV antibiotics, history of prior pseudomonal infection, immunocompromised (uncontrolled HIV, transplant, etc.)

References:

2. Hooton, Thomas M., et al. "Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America." Clinical infectious diseases 50.5 (2010): 625-663.

<sup>1.</sup> Gupta, Kalpana, et al. "International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases." Clinical infectious diseases 52.5 (2011): e103-e120.

## **Community Acquired Pneumonia (CAP)**

#### Diagnosis

Requires the presence of clinical features (cough, fever, sputum production, pleuritic chest pain) AND chest infiltrate demonstrated on imaging

#### **Common Causative Organisms**

Streptococcus pneumoniae, Mycoplasma pneumoniae, Chlamydia pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, Respiratory viruses

#### **Outpatient Empiric CAP Treatment**

Previously healthy	Doxycycline 100 mg PO BID (preferred)
AND	OR
no antibiotics in the past 3 months	Amoxicillin 1 gm PO TID (alternative)
Antibiotic use in prior 3 months	Combination Therapy (preferred):
OR	Doxycycline 100 mg PO BID
Presence of co-morbidities	PLUS
Immunosuppression	Amoxicillin 1 gm PO TID
• Chronic heart, lung, liver, or renal disease	OR
Diabetes mellitus	Cefpodoxime 200 mg PO BID
Alcoholism	
Malignancy	
Asplenia	Monotherapy (alternative)
	Levofloxacin* 750 mg PO daily

\* Contact ASP PharmD (preferred) or ID fellow for approval unless patient has severe penicillin allergy

#### Suggested Duration of Therapy

- Patients should be treated for a minimum of 5 days
- Most patients are treated for 5-7 days

#### **Clinical Pearls**

- Routine sputum cultures and urine antigen tests are not recommended
- Consider testing for influenza and COVID-19 if patient exhibits flu-like symptoms during periods of high flu and SARS-CoV-2 activity
- Signs and symptoms of CAP may be lacking or altered in elderly patients
- Cough and chest X-ray abnormalities may take up to 6 weeks to improve and are NOT a valid reason to extend antibiotic courses

#### Inpatient Empiric CAP Treatment



#### **Suggested Duration of Therapy**

- Patients should be treated for a minimum of 5 days unless the patient has confirmed MRSA or *Pseudomonas aeruginosa* infection in which case the minimum duration is 7 days
- Azithromycin 500 mg PO/IV q24h x **3 doses** is sufficient for atypicals; if *legionella* is suspected treat for 7 days
- Patient should be afebrile for 48-72h, and should have no more than 1 of the following before stopping antibiotics:
  - Heart rate > 100 beats/min
  - Respiratory rate > 24 breaths/min
  - Systolic blood pressure < 90 mmHg</li>
  - Arterial O2 saturation < 90%
  - o Altered mental status

#### **Clinical Pearls**

- Sputum cultures should be obtained for hospitalized patients with severe CAP or when strong risk factors for MRSA or *Pseudomonas* are identified
- MRSA nares should be obtained if empiric vancomycin therapy is initiated for pneumonia to assist with de-escalation (strong negative predictive value)
- For suspected influenza, obtain nasopharyngeal swabs for influenza antigen testing and respiratory virus DFA; if patient is
  hospitalized, place on droplet precautions until tests are negative, and treat with oseltamivir 75 mg PO bid for 5 days (reduce
  dose in renal insufficiency). ICU patients, immunocompromised patients, and obese patients may require higher doses and/or
  prolonged therapy.

References: Metlay, Joshua P., et al. "Diagnosis and treatment of adults with community-acquired pneumonia. An official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America." American journal of respiratory and critical care medicine 200.7 (2019): e45-e67.

## Hospital Acquired Pneumonia (HAP) and Ventilator Associated Pneumonia (VAP)

Antibiotic dosing for HAP/VAP (refer to IV antimicrobial dosing section for renal dose adjustments and vancomycin dosing/monitoring guidance)

- Piperacillin/tazobactam (pip/tazo) 4.5 gm IV q6h
- Cefepime 2 gm IV q8h
- Ceftriaxone 2 gm IV q24h
- Vancomycin 20 mg/kg IV one-time loading dose + maintenance dose targeting AUC 500-600 mg\*h/L
- Aztreonam 2 gm IV q8h
- Levofloxacin 750 mg IV/PO q24h

#### Empiric Treatment WITH respiratory culture gram stain results available (i.e., BAL, tracheal aspirate, sputum, etc.)

Diagnosis	Antibiotic Regimens	Alternative Drug(s)	Comments	Expected Duration
HAP and VAP <u>With gram</u> <u>stain</u> <u>available</u> within 72 hours	Start: pip/tazo* <u>OR</u> ceftriaxone +/-vancomycin         Consider ceftriaxone: if no risk         factors for Pseudomonas (see         comments), short duration of         intubation (i.e., < 5 days),	Mild-moderate penicillin allergy:         Cefepime* +/- vancomycin         Severe penicillin allergy:         Aztreonam OR Levofloxacin* +/         Vancomycin^         Antibiotics based on respiratory         culture gram stain findings for         patients with severe allergy         precluding use of a cephalosporin: <ul> <li>GP rods: vancomycin</li> <li>GPC in pairs/chains:</li> <li>levofloxacin</li> <li>GPC in clusters:</li> <li>vancomycin</li> <li>GNRs: aztreonam* or</li> <li>levofloxacin</li> <li>No organisms:</li> <li>vancomycin +</li> <li>aztreonam* or</li> <li>levofloxacin. Stop</li> <li>antibiotics if concern for</li> <li>pneumonia is low.</li> </ul>	Consider coverage for MRSA and/or Pseudomonas aeruginosa in patients with: respiratory isolation of these organisms or receipt of parenteral antibiotics within 90 days, admitted from skilled nursing or other long term care facility after at least one week stay. If these organisms are not isolated from clinical cultures (e.g. blood cultures), deescalate antibiotics. Consider withholding empiric vancomycin in patients with neg MRSA nares culture within prior 7 days. Stop vancomycin at 48 hours if MRSA nares culture/PCR is negative and/or no MRSA isolated from clinical cultures. A positive MRSA nares culture/PCR indicates that the patient is colonized with MRSA. Patients with a positive MRSA nares culture/PCR should be initiated on empiric anti-MRSA therapy (vancomycin). However, antibiotics should be tailored to respiratory gram stain & culture results. Stop vancomycin at 48 hours if no MRSA isolated from clinical cultures. Antibiotic use at the time of respiratory culture collection may decrease gram stain yield. Contact ID pharmacy/ID consult with questions. For patients with known respiratory colonization with multidrug resistant organisms (MDRO) consider empiric coverage of these organisms pending culture results	7 days

\*Contact ASP Pharmacist or ID Fellow for approval (pip/tazo and cefepime do not need approval in the ICU)

#### Empiric Treatment WITHOUT respiratory culture gram stain results available

Diagnosis	Antibiotic Regimens	Alternative Drug(s)	Comments	Expected Duration
HAP Hemodynamically stable NOT on high-flow nasal cannula Including patients with HAP due to aspiration	Start: Ceftriaxone Consider pip/tazo OR cefepime if risk factors for <i>Pseudomonas</i> (see comments) or Risk factors for <i>Pseudomonas</i> or resistant GNRs: Pip/tazo	<u>Mild-moderate penicillin</u> <u>allergy:</u> Cefepime* <u>Severe penicillin allergy:</u> Aztreonam OR levofloxacin*	Consider empiric vancomycin if clinical concern for MRSA pneumonia (e.g., necrotizing pneumonia on imaging). If starting vancomycin, collect MRSA nares culture/PCR. Consider coverage for MRSA and/or <i>Pseudomonas aeruginosa</i> in patients with respiratory isolation of these organisms or receipt of parenteral antibiotics within 90 days, admitted from skilled nursing or other long term care facility after at least one week stay. If these organisms are not isolated from clinical cultures (e.g. blood cultures), deescalate antibiotics.	7 days
VAP and HAP <u>with</u> ICU level care/ High- flow nasal cannula	Start: pip/tazo* OR ceftriaxone +/- vancomycin <u>Consider ceftriaxone</u> : if no risk factors for Pseudomonas (see comments), short duration of intubation (i.e., < 5 days), hemodynamically stable	<u>Mild-moderate penicillin</u> <u>allergy:</u> Cefepime* +/- vancomycin <u>Severe penicillin allergy:</u> Aztreonam OR Levofloxacin* +/ Vancomycin^	Consider withholding empiric vancomycin in patients with neg MRSA nares culture within prior 7 days. Consider coverage for MRSA and/or Pseudomonas aeruginosa in patients with respiratory isolation of these organisms or receipt of parenteral antibiotics within 90 days, admitted from skilled nursing or other long term care facility after at least one week stay. If these organisms are not isolated from clinical cultures (e.g., blood cultures), deescalate antibiotics. Stop vancomycin at 48 hours if admission MRSA nares is negative and/or no MRSA	7 days

\*Contact ASP Pharmacist or ID Fellow for approval (pip/tazo and cefepime do not need approval in the ICU)

# Role and Interpretation of Methicillin-Resistant S. aureus (MRSA) Nares Results in Context of Hospital-Acquired and Ventilator-Associated Pneumonia (HAP/VAP)

Collecting a MRSA nares culture/PCR is recommended for all patients initiating anti-MRSA therapy (e.g. vancomycin) for suspected HAP or VAP.

#### How to interpret a negative MRSA nares result in patient with possible HAP/VAP:

A negative MRSA nares culture or PCR indicates the patient is less likely to be colonized with MRSA. Multiple studies indicate that a negative MRSA nares culture or PCR carries a high negative predictive value for MRSA pneumonia (> 95%),<sup>3-6</sup> even when collected prior to onset of pneumonia.<sup>3,5</sup> If a patient's MRSA nares is negative, their likelihood of having MRSA pneumonia is exceedingly low and anti-MRSA therapy (e.g. vancomycin) can reasonably be discontinued or withheld.

#### How to interpret a positive MRSA nares result in patient with possible HAP/VAP:

A positive MRSA nares culture or PCR indicates that the patient is colonized with MRSA. Patients with a known positive MRSA nares culture/PCR who develop a HAP or VAP should be initiated on antibiotics including empiric anti-MRSA therapy (e.g. vancomycin). However, antibiotics should be tailored to respiratory gram stain & culture results. Stop vancomycin at 48 hours if no MRSA isolated from clinical cultures. If a patient's MRSA nares culture or PCR results positive after the patient has been started on antibiotics to treat HAP/VAP, no change in therapy is recommended (in other words – no need to add empiric anti-MRSA therapy) provided the patient is stable and clinically improving.

## Intra-abdominal Infections (IAI)

- Intra-abdominal infections are those contained within the peritoneal cavity or retroperitoneal space.
- May be generalized or localized, complicated or uncomplicated, and community or healthcare-associated



Complicated appendicitis patients after undergoing appendectomy

24-48 hours

## **Clostridioides difficile Infection (CDI)**

#### Order menus available for ambulatory care, inpatient, ED, and CLC

Clinical Definitio	n Supportive Clinical Data
Asymptomatic colonizat	tion Positive C. difficile PCR (only) WITHOUT diarrhea, ileus, or colitis
Active infection	Diarrhea (3+ unformed stools within 24 hours) AND either
	- Positive <i>C. difficile</i> PCR <b>AND</b> positive toxin A/B
	OR     Presence of pseudomembranous colitis on colonoscopic or histopathologic exam
Recurrent infection	Active infection that occurs within 8 weeks after completing treatment of prior CDI episode
Fulminant	Active infection PLUS hypotension, shock, ileus, megacolon, or perforation
CDI Treatment Regime	ens
v	Vancomycin 125 mg PO q6h for 10 days OR
Initial episode	Fidaxomicin 200 mg PO q12h for 10 days for patients at increased risk of CDI recurrence:
	<ul> <li>Age &gt; 65 years old, immunosuppression, history of inflammatory bowel disease</li> </ul>
	<ul> <li>Concomitant antibiotic use during CDI treatment</li> </ul>
1 <sup>st</sup> Recurrence	Fidaxomicin 200 mg PO q12h for 10 days
1 neourielle	Vancomycin taper: Vancomycin 125mg PO q6h x14 days, then 125mg PO q12h x7 days, then 125mg PO
	daily x7 days, then 125mg PO every other day x7 days, then 125mg PO quarky days, then 125mg PO every other day x7 days, then 125mg every 3 <sup>rd</sup> day x14 days
≥ 2 <sup>nd</sup> Recurrence	PLUS
	ID or GI consult for fecal microbiota transplant (FMT) evaluation (i.e., VOWST)
	Vancomycin oral solution 500mg PO q6h
	<ul> <li>If ileus is present, add metronidazole 500mg IV q8h and consider Vancomycin 500 mg in 100 mL</li> </ul>
Fulminant	normal saline given as a retention enema q6h
raininant	<ul> <li>Therapy should be followed by a vancomycin taper (see above)</li> </ul>
	<ul> <li>ID or GI and surgical consultation should be obtained for severely ill patients</li> </ul>
CDI Pronhylavic Agont	
CDI Prophylaxis Agent	Must meet ALL of the following criteria:
Vancomycin	
125 mg PO q12h	······································
	Patient requires treatment with antibiotics (beta-lactams, quinolones, or clindamycin) not directed
	against CDI in the inpatient setting
	No history of vancomycin allergy
	Initiate as soon as possible and continue until antibiotics not directed against CDI are discontinued
	Must meet ALL of the following criteria:
	At least 2nd recurrent CDI (3rd CDI episode overall) within previous 12 months
	At least one CDI episode was treated with fidaxomicin, unless not tolerated or contraindicated
VOWST™ (FMT)	Is able to start VOWST within 2 to 4 days after completing of current CDI treatment
	Patients are <u>ineligible if ONE</u> of the following criteria are met:
ID or GI section	Asymptomatic C. difficile colonization (i.e., patient is not on therapy for active CDI prior to VOWST)
approval is required	• ANC < 500 cells/m <sup>3</sup>
approvaris required	Is likely to require systemic antibiotics or pre-op antibiotics within 8 weeks after VOWST treatment
Place pharmacy non-	• Inability to use magnesium citrate or polyethylene glycol or take VOWST prior to first meal of day
formulary drug	Pretreatment:
consult (PADR)	Take 296 mL magnesium citrate 8 hours prior to first dose of VOWST
consult (FADR)	<ul> <li>If renal impairment, prescribe 250 mL polyethylene glycol</li> </ul>
	Treatment:
	Avoid eating or drinking, except for small amounts of water, for at least 8 hours prior to first dose

#### **Clinical Pearls**

- If an inciting antimicrobial is suspected discontinue the agent as soon as possible.
- The use of antimotility agents (loperamide, etc.) should be avoided.
- If severe or fulminant disease is suspected, initiate empiric treatment while awaiting assay results. If the assay is negative, use clinical judgment when deciding if therapy should be discontinued.
- Use caution with high dose oral/rectal vancomycin (500mg Q6H) in patients with renal insufficiency, as significant absorption can occur in the setting of colitis and systemic accumulation could lead to ototoxicity, nephrotoxicity, or other adverse effects.
- Always wash hands with soap and water after examining a patient with suspected/confirmed C. difficile, as alcohol-based sanitizers do NOT kill spores.
- Fidaxomicin and vancomycin PO are ONLY orderable through the CDI order menus (inpatient, CLC, ED, and ambulatory care)

## **Guidelines for Blood Culture Identification (BCID) 2 Data**

#### What is BCID2?

The BioFire<sup>®</sup> FilmArray<sup>®</sup> Blood Culture Identification Panel (BCID) 2 is a test used to rapidly identify pathogens by amplifying DNA through PCR. This laboratory method helps identify organisms and resistance genes from positive blood cultures. **Table 1** lists the bacterial and fungal pathogens, and resistance genes detected by the BCID2 panel.

#### Table 1: BCID2 Pathogen and Resistance Gene Panel

Gram-Positive Bacteria	Gram-Negative Bacteria	Yeast	Resistance Genes
Enterococcus faecalis	Acinetobacter baumannii complex	Candida albicans	Carbapenemases
Enterococcus faecium	Bacteroides fragilis	Candida auris	- IMP
Listeria monocytogenes	Enterobacterales Order	Candida glabrata	- KPC
Staphylococcus genus	- Enterobacter cloacae complex	Candida krusei	- OXA-48-like
- Staphylococcus aureus	- Escherichia coli	Candida parapsilosis	- NDM
- Staphylococcus epidermidis	- Klebsiella aerogenes	Candida tropicalis	- VIM
- Staphylococcus lugdunensis	- Klebsiella oxytoca	Cryptococcus	Colistin Resistance
Streptococcus genus	- Klebsiella pneumoniae group	neoformans/gatti	- mcr-1
- Streptococcus agalactiae	- Proteus spp.		ESBL
- Streptococcus pneumoniae	- Salmonella spp.		- CTX-M
- Streptococcus pyogenes	- Serratia marcescens		Methicillin-resistance
	Haemophilus influenzae		- mecA/C
	Neisseria meningitidis		<ul> <li>mecA/C and MREJ (MRSA)</li> </ul>
	Pseudomonas aeruginosa		Vancomycin Resistance
	Stenotrophomonas maltophilia		- vanA/B

#### How is BCID2 incorporated into clinical practice?

The microbiology lab notifies clinicians of positive blood culture gram-stain results immediately after they are performed. Afterwards, the BCID2 assay is performed for rapid identification. BCID2 results are typically available in CPRS within 2 hours. When blood culture gram stain and BCID2 results are known, current antimicrobial therapy should be evaluated considering the clinical picture and adjusted to the most appropriate single agent if possible. Recommended empiric antibiotic therapies for BCID2 results are outlined in **Tables 2-4** for gram-positive bacteria, gram-negative bacteria, and fungi. The Antimicrobial Stewardship Team developed these recommendations based on an analysis of the institutional antibiogram and IDSA Clinical Guidelines. Contact the ASP Pharmacist for alternative recommendations if patient is not a candidate for first line therapy. All dosing recommendations assume normal renal or hepatic function, pleas adjust dosing accordingly.

# ASP/ ID support for BCID2 Results



\*High risk organisms: Staphylococcus aureus, Enterococcus spp., fungi, and carbapenem resistant organisms

#### How reliable are BCID2 results?

The BCID2 test is highly accurate in monomicrobial bacteremia (99% sensitivity and 99.8% specificity), but in the rare incidence of polymicrobial bacteremia it may be less accurate. Therefore, polymicrobial gram stain results and BCID2 results with multiple organisms detected should be interpreted with caution. On the other hand, certain infections may be polymicrobial in nature and the isolation of a single pathogen from blood cultures, while allowing narrowing of therapy, should not result in over-narrowing. An example would be complicated intra-abdominal infections where anaerobes are frequently present and therapy active against these pathogens should generally be included until definitive cultures of the site of infection have returned.

BCID2 identification is limited to the pathogens and resistance genes listed on the panel (**Table 1**). If a positive blood culture results in a negative BCID2 report, please contact ASP Pharmacist or ID team for guidance. Occasionally, the detection of a resistance gene does not equate to confirmation of resistance when susceptibility testing is performed. Standard susceptibility testing is required to determine final antimicrobial susceptibility and should be used to guide final therapy decisions. When full susceptibility results become available, therapy should be adjusted to the narrowest spectrum appropriate agent.

#### References:

 Rhoads DD, Pournaras S, Leber A, et al. Multicenter Evaluation of the BIOFIRE Blood Culture Identification 2 Panel for Detection of Bacteria, Yeasts, and Antimicrobial Resistance Genes in Positive Blood Culture Samples. *J Clin Microbiol* 2023; 61(6): e0189122.
 IDSA 2023 Guidance on the Treatment of Antimicrobial Resistant Gram-Negative Infections (idsociety.org)

Bacterial Marker	Result	Interpretation	Preferred Therapy/ Comments
Enterococcus faecalis VanA/B	Detected Not Detected	Enterococcus faecalis Not-VRE	Ampicillin 2 gm IV q4h Infectious diseases (ID) service auto-consulted per hospital
			policy
Enterococcus faecalis VanA/B	Detected Detected	Enterococcus faecalis VRE (uncommon)	Ampicillin 2 gm IV q4h
		. ,	ID service auto-consulted per hospital policy
Enterococcus faecium	Detected	Enterococcus faecium	Vancomycin* IV one-time loading dose + maintenance dose
VanA/B	Not Detected	Not-VRE (uncommon)	(see pages 44-45 for dosing and monitoring
			ID service auto-consulted per hospital policy
Enterococcus faecium VanA/B	Detected Detected	Enterococcus faecium VRE	Daptomycin <sup>10-12</sup> mg/kg IV q24h
-			ID service auto-consulted per hospital policy
Listeria monocytogenes	Detected	Listeria monocytogenes	Ampicillin 2 gm IV q4h
Staphylococcus	Detected	Possible Methicillin-	Vancomycin* IV one-time loading dose + maintenance dose
S. aureus	Detected Not Detected	susceptible S. aureus	(see pages 44-45 for dosing and monitoring)
S. epidermidis, S. lugdunensis MREJ and mecA/C	N/A	(MSSA)	Presume MRSA until final susceptibilities available due to high
			incidence of underdetection with this species
			ID service auto-consulted per hospital policy
Staphylococcus	Detected	Methicillin-resistant S.	Vancomycin* IV one-time loading dose + maintenance dose
S. aureus	Detected	aureus (MRSA)	(see pages 44-45 for dosing and monitoring)
S. epidermidis, S. lugdunensis MREJ and mecA/C	Not Detected Detected		ID service auto-consulted per hospital policy
Staphylococcus	Detected	Methicillin-susceptible	1 of 2 blood culture sets positive: likely contaminant
S. epidermidis	Detected	Staphylococcus	Do not start antibiotics
S. aureus, S. lugdunensis mecA/C	Not Detected Not Detected	epidermidis (MSSE)	If severely ill and on antibiotics, continue current therapy until definitive results become available
			2 of 2 blood culture sets positive: possible infection Cefazolin 2 gm IV q8h
Staphylococcus	Detected	Methicillin-resistant	Blood culture results:
S. epidermidis	Detected	Staphylococcus	1 of 2 sets positive: likely contaminant
S. aureus, S. lugdunensis	Not Detected	epidermidis (MRSE)	Do not start antibiotics
mecA/C	Detected		<ul> <li>If severely ill and on antibiotics, continue current therapy until definitive results become available</li> </ul>
			2 of 2 sets positive: possible infection
			Vancomycin* IV one-time loading dose + maintenance dose (see pages 44-45 for dosing and monitoring
			Used purpose in the dosing and monitoring

#### Table 2: Gram-Positive Bacteria

apy/ Comments
<sup>7</sup> q8h ult ulase-negative species, infections are more like 2 blood culture sets positive, may be a t favor treatment and repeating blood cultures
one-time loading dose + maintenance dose for dosing and monitoring ult Jase-negative species, infections are more like 2 blood culture sets positive, may be a t favor treatment and repeating blood cultures
are sets positive: likely contaminant t start antibiotics erely ill and on antibiotics, continue current by until definitive results become available are sets positive: possible infection one-time loading dose + maintenance dose for dosing and monitoring
ion units IV q4h gm IV q24h
n: Ceftriaxone 2 gm IV q24h ftriaxone 2 gm IV q12h + e-time loading dose + maintenance dose for dosing and monitoring
ion units IV q4h gm IV q24h
ure sets positive: likely contaminant der withholding antibiotics erely ill and on antibiotics, continue current by until definitive results become available ure sets positive: possible infection

\* Contact team pharmacist/ inpatient pharmacy for assistance with vancomycin target achievement (AUC and/or trough) ^ Contact ASP Pharmacist or ID fellow is unavailable for antibiotic approval

#### Table 3: Gram-Negative Bacteria

Bacterial Marker	Result	Interpretation	Preferred Therapy/ Comments
Acinetobacter calcoaceticus-baumannii	Detected	Acinetobacter calcoaceticus-	Ampicillin-sulbactam 3 gm IV q6h
complex		baumannii complex	
IMP, KPC, NDM, VIM	Not Detected		
CTM-X	Not Detected		
Acinetobacter calcoaceticus-baumannii	Detected	Presumed carbapenem-resistant	KPC:
complex		Acinetobacter calcoaceticus-	Ampicillin-sulbactam 3 gm IV q4h
IMP, KPC, NDM, VIM	Detected	baumannii complex	+ Minocycline <sup>^</sup> 200 mg IV/PO q12h
CTM-X	Not Detected		
			IMP, NDM, or VIM:
			Ampicillin-sulbactam 3 gm IV q4h
			+ Minocycline <sup>^</sup> 200 mg IV/PO q12h
			+ Cefiderocol^ 2 gm IV q6h
			ID service auto-consulted per policy
Acinetobacter calcoaceticus-baumannii	Detected	Presumed beta-lactamase	Meropenem <sup>^</sup> 2 gm IV q8h
complex		producing	
IMP, KPC, NDM, VIM	Not Detected	Acinetobacter calcoaceticus-	
CTM-X	Detected	baumannii complex	
Bacteroides fragilis	Detected	Bacteroides fragilis (anaerobe)	Metronidazole 500 mg IV/PO q8h
Haemophilus influenzae	Detected	Haemophilus influenzae	Ampicillin-sulbactam 3 gm IV q6h

Bacterial Marker	Result	Interpretation	Preferred Therapy/ Comments		
Neisseria meningitidis (encapsulated) Detected		Neisseria meningitidis	Ceftriaxone 2 gm IV q12h		
Pseudomonas aeruginosa IMP, KPC, NDM, VIM CTM-X	Detected Not Detected Not Detected	Pseudomonas aeruginosa	Piperacillin-tazobactam^ 4.5 gm IV q6h or Cefepime^ 2 gm IV q8h <u>KPC</u> : Ceftazidime-avibactam^ 2.5 gm IV q8h <u>IMP, NDM, VIM:</u> Cefiderocol^ 2 gm IV q6h		
Pseudomonas aeruginosa IMP, KPC, NDM, VIM CTM-X	Detected Detected Not Detected	Presumed carbapenem-resistant Pseudomonas aeruginosa			
Pseudomonas aeruginosa IMP, KPC, NDM, VIM	Detected Not Detected	Presumed beta-lactamase producing	ID service auto-consulted per policy Non-CNS: Meropenem <sup>1</sup> gm IV q8h		
CTM-X Stenotrophomonas maltophilia	Detected Detected	Pseudomonas aeruginosa Stenotrophomonas maltophilia	CNS: Meropenem <sup>2</sup> gm IV q8h TMP/SMX 5 mg/kg (of TMP component) IV/PO q12h + Levofloxacin <sup>7</sup> 750 mg IV/PO q24h		
The following guidelines are in reference	e to BCID2 results p	ositive for the <u>Enterobacterales</u> o			
Results and interpretation for resistance					
Bacterial Marker	Result	Interpretation	Preferred Therapy/ Comments		
Enterobacterales Enterobacter cloacae complex Escherichia coli, Klebsiella aerogenes,	Detected Detected Not Detected	Enterobacter cloacae complex	Ertapenem 1 gm IV q24h Inducible AmpC beta-lactamase producer – carbapenems are drug of choice		
Klebsiella oxytoca, Klebsiella pneumoniae group, Proteus spp., Salmonella spp., Serratia marcescens					
Enterobacterales Escherichia coli	Detected Detected	Escherichia coli	Ceftriaxone 2 gm IV q24h		
Enterobacter cloacae complex, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae group, Proteus spp., Salmonella spp., Serratia marcescens	Not Detected				
Enterobacterales	Detected	Klebsiella aerogenes	Ertapenem 1 gm IV q24h		
Klebsiella aerogenes Enterobacter cloacae complex, Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae group, Proteus spp., Salmonella spp., Serratia marcescens	Detected Not Detected		Inducible AmpC beta-lactamase producer – carbapenems are drug of choice		
Enterobacterales Klebsiella oxytoca	Detected Detected	Klebsiella oxytoca	Ceftriaxone 2 gm IV q24h		
Enterobacter cloacae complex, Escherichia coli, Klebsiella aerogenes, Klebsiella pneumoniae group, Proteus spp., Salmonella spp., Serratia marcescens	Not Detected				
Enterobacterales Klebsiella pneumoniae group	Detected Detected	Klebsiella pneumoniae group	Ertapenem 1 gm IV q24h Antibiogram 2024: 19% of isolates were		
Enterobacter cloacae complex, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Proteus spp., Salmonella spp., Serratia marcescens	Not Detected		ESBL positive and may not be mediated through CTM-X gene		
Enterobacterales Proteus spp.	Detected Detected	Proteus spp.	Ceftriaxone 2 gm IV q24h		
Enterobacter cloacae complex, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae group, Salmonella spp., Serratia marcescens	Not Detected				

Bacterial Marker	Result	Interpretation	Preferred Therapy/ Comments		
Enterobacterales	Detected	Salmonella spp.	Ceftriaxone 2 gm IV q24h		
Salmonella spp.	Detected				
Enterobacter cloacae complex,	Not Detected				
Escherichia coli, Klebsiella aerogenes,					
Klebsiella oxytoca,					
Klebsiella pneumoniae group,					
Proteus spp., Salmonella spp.					
Enterobacterales	Detected	Serratia marcescens	Ertapenem 1 gm IV q24h		
Serratia marcescens	Detected				
Enterobacter cloacae complex,	Not Detected				
Escherichia coli, Klebsiella aerogenes,					
Klebsiella oxytoca,					
Klebsiella pneumoniae group,					
Proteus spp., Serratia marcescens					
Enterobacterales	Detected	Enterobacterales organism not	Ertapenem 1 gm IV q24h		
		listed on BCID2 panel			
Enterobacter cloacae complex	Not Detected		Consider ID consult		
Escherichia coli, Klebsiella aerogenes,					
Klebsiella oxytoca, Klebsiella pneumoniae					
group, Proteus spp., Salmonella spp.,					
Serratia marcescens					
Enterobacterales	Detected	Presumed Beta-lactamase	Ertapenem 1 gm IV q24h		
Any species	Detected	producing (ESBL)			
Resistance genes:		Enterobacterales			
CTM-X	Detected				
IMP, KPC, NDM, VIM, OXA-48 -like	Not Detected				
mcr-1	Not Detected				
Enterobacterales	Detected	Presumed Carbapenem resistant	ID service auto-consulted per policy		
Any species	Detected	Enterobacterales			
Resistance genes:					
CTM-X	Not Detected				
IMP, KPC, NDM, VIM, OXA-48 -like	Detected				
mcr-1	Not Detected				
Enterobacterales	Detected	Presumed Colistin resistant	If mcr-1 is the only resistance gene		
Any species	Detected	Enterobacterales	identified, continue empiric therapy for		
Resistance genes:			isolated organisms		
CTM-X	Not Detected				
IMP, KPC, NDM, VIM, OXA-48 -like	Not Detected		If more than 1 resistance gene present,		
mcr-1 Contact ASP Pharmacist for antibiotic approval	Detected		consider ID consult for guidance		

^Contact ASP Pharmacist for antibiotic approval

#### Table 4: Fungal Pathogens

Bacterial Marker	Result	Interpretation	Preferred Therapy/ Comments
Candida albicans	Detected	Candida albicans	Fluconazole 12 mg/kg IV/PO once, then 6 mg/kg q24h IV/PO
Candida auris	Detected	Candida auris	Micafungin 100 mg IV q24h
Candida glabrata	Detected	Candida glabrata	Micafungin 100 mg IV q24h
Candida krusei	Detected	Candida krusei	Micafungin 100 mg IV q24h
Candida parapsilosis	Detected	Candida parapsilosis	Micafungin 100 mg IV q24h
Candida tropicalis	Detected	Candida tropicalis	Micafungin 100 mg IV q24h
Cryptococcus neoformans/gatti	Detected	Cryptococcus neoformans/gatti	Amphotericin B (liposomal) 3-4 mg/kg IV q24h +/- flucytosine 25 mg/kg PO q6h

All fungal pathogens isolated in the blood will trigger an automatic ID consult per hospital policy

## Non-Purulent Skin and Soft Tissue Infections (SSTI)

Order menu available for inpatient and ED



with baseline elevations in serum potassium or creatinine
 who are taking an ARB/ACEi or spironolactone

## Purulent Skin and Soft Tissue Infections (SSTI)

#### Order menu available for inpatient and ED



## **Recurrent Skin and Soft Tissue Infections (SSTI)**



Injection Drug Use Guidance:

- Wash hands before injection and sterilize injection sites

- Do not share needles, do not lick needles

## Vaccines for Adults With Splenectomy

	Highly Recommended Vaccines				May Consider for Specific Populations		
٠	COVID-19	٠	Pneumococcal (conjugate, 20-	•	Hepatitis A (HAV)	•	MMR
•	Hib		valent)	•	Hepatitis B (HBV)	٠	Мрох
•	Influenza	٠	RSV	•	HPV	٠	Varicella
•	Meningococcal (conjugate &	•	Tdap				
	serogroup B)	٠	Zoster				

#### Timing of Vaccine Administration Relative to Splenectomy

Pre-operation	Post-operation
• Complete vaccination > 2 weeks prior to	• If vaccination series cannot be initiated prior to splenectomy, start at least 14
procedure.	days after surgery or prior to discharge, whichever comes first
• For vaccination series with <b>multiple</b>	• If vaccines were administered prior to postoperative day 14 (sooner than 2
doses: INITIATE ~10-12 weeks prior to	weeks post-operative): Repeat the vaccines 8 weeks AFTER the initial doses
splenectomy, so recommended series can	were given.
be <u>COMPLETED &gt; 2 weeks</u> prior to	<ul> <li>Patients receiving other immunosuppressive treatment following splenectomy:</li> </ul>
procedure.	The vaccination schedule is further modified. For example, <b>resumption of</b> vaccines ~3 months after treatment has been reported.

#### Vaccination Schedule

	vaccination Schedule						
	Highly Recommended Vaccines	5					
Dose #1	Dose #2	Boosters					
COVID-19	See <u>Clinical Guidance for COVID-19 Vaccination</u> for up-to-date recommendations. Local						
	guidance can be found SFVAHCS	COVID-19 Vaccine Resources					
HAEMOPHILUS B CONJUGATE (Hib)	N/A	N/A					
INFLUENZA (1 dose annually)	N/A	N/A					
MENINGOCOCCAL OLIGOSACCHARIDE CONJUGATE	≥ 8 weeks after dose 1	Every 5 years					
[MenACWY-CRM] (MENVEO)		(off-label for ages >55)					
MENINGOCOCCAL B [MenB-4C] (BEXSERO)	≥ 4 weeks after dose 1	1 year after completion of primary series, then every					
		2-3 years thereafter					
PNEUMOCOCCAL	N/A series completed after PCV	N/A					
1. Received PCV 20 $\rightarrow$ series completed	20						
2. Vaccine naïve → administer PCV 20							
3. Received PPSV 23 only $\rightarrow$ administer PCV 20							
RSV [ <b>age ≥75,</b> or <b>age 60-74 + risk factor</b> ]	N/A	N/A					
DIPHTHERIA / PERTUSSIS / TETANUS (Tdap)	N/A	Every 10 years					
ZOSTER RECOMBINANT (Shingrix) [age > 50]	2-6 months after dose 1	N/A					
	Additional Vaccines to Conside	r					
Dose #1	Dose #2	Dose #3					
HEPATITIS A (HAVRIX) <sup>+</sup>	6-12 months after dose 1	N/A					
HEPATITIS B RECOMBINANT (ENGERIX-B) <sup>‡</sup>	1 month after dose 1	6 months after dose 1					
PAPILLOMAVIRUS HUMAN 9-VALENT (GARDASIL 9)	$\geq$ 4 weeks after dose 1	≥ 4 weeks after dose 2					
MPOX <mark>*</mark>	4 weeks after dose 1	N/A					
MEASLES, MUMPS, AND RUBELLA (MMR)	>1 month after dose 1 in select	N/A					
	patients						
VARICELLA VIRUS (VARIVAX)	> 4-8 weeks after dose 1	N/A					
Service restricted	1						

#### \*Service restricted

<sup>†</sup>**Risk factors for HAV:** International travelers, men who have sex with men, and individuals who use/inject illicit drugs, with occupational risk for exposure, who anticipate close contact with an international adoptee, and experiencing homelessness.

\*Risk factors for HBV: Infants born to mothers with HBV, individuals who inject drugs or share needles, sex partners of individuals with HBV, men who have sex with men, individuals who live with someone who has HBV, health care and public safety workers exposed to blood on the job, and people on dialysis.

## **Beta-Lactam Test Dosing Protocol**

#### WHAT IS BETA-LACTAM TEST DOING?

A formalized process for evaluating patients with reported beta-lactam allergies. Those that are determined as low risk for an adverse reaction with a different beta-lactam antibiotic from their initial allergy, will receive a one-time test dose (10% of their full treatment dose) of an alternative beta-lactam under observation. If the patient tolerates this, they will receive a full dose (100% of treatment dose) 30 minutes later. If the patient tolerates both doses, they will continue on this antibiotic to treat their infection.

#### WHY ARE WE DOING THIS?

- Cross-Reactivity rates between different beta-lactam antibiotics are low. Therefore, patients with true penicillin or cephalosporin allergies can still receive many other cephalosporins and carbapenems
- By evaluating patients through a thorough allergy assessment, we can identify patients at low risk of having an adverse reaction with alternative beta-lactams which will allow the patient to receive a more effective, less toxic, and/or less costly antibiotics to treat their infections.

#### HOW ARE WE DOING THIS?

- A new order set is available to standardize the test dose, full dose, assessment, and monitoring
- Primary team can order Beta-Lactam Test Doses via the order set for eligible inpatients with a reported beta-lactam allergy AND an active infection in which a beta-lactam is indicated for treatment
- Case will be review by ID Pharmacist (pager: 415-223-8046) prior to proceeding
- Test doses will be conducted Monday through Friday from 10:00 to 14:00
- For patients with a history of severe, IgE mediated reactions, test doses should be administered in the TCU. All other patients may undergo this protocol outside of the TCU.
- If possible, systemic beta-blocker doses should be held for 24 hours prior to test dose
- Monitoring nurse will use new CPRS template to document vital signs obtained after doses

#### WHAT MEDICATIONS ARE NEEDED FOR THIS PROCESS?

#### Order set available for inpatient use

- Pharmacy will send the antibiotic test dose and the Rescue Medication Kit that will include:
  - Epinephrine 0.3 mg pen x1
  - 0.9% NS 1 L bag x1
  - Diphenhydramine 50 mg vial x1
  - Methylprednisolone 125 mg vial x1
  - Glucagon 1 mg vial x1
  - Albuterol 0.083% 3 mL vials x2
- The full dose may be located in the pyxis machine or will be delivered by pharmacy

## Overview of Beta-Lactam Test Dose Protocol



## Penicillin Allergy Pathway for Beta-Lactam Test Dose



## **Cephalosporin Allergy Pathway for Beta-Lactam Test Dose**



# Beta-Lactam Cross Reactivity Table

					Pe	nicilli	ins			Cephalosporins							Mono								
											1st			2nd				3rd			4th		5th		
			Nafcillin	Oxacillin	Dicloxacillin	Penicillin G/VK	Piperacillin	Ampicillin	Amoxicillin	Cefadroxil	Cephalexin	Cefazolin	Cefoxitin	Cefuroxime	Cefotetan	Cefdinir	Cefixime	Ceftriaxone	Cefpodoxime	Ceftazidime	Cefepime	Ceftaroline	Ceftolozane	Cefiderocol	Aztreonam
		Nafcillin																							
		Oxacillin																							
lins		Dicloxacillin																							
Penicillins		Penicillin G/VK																							
en		Piperacillin																							
<b>_</b>		Ampicillin																							
		Amoxicillin																							
		Cefadroxil																							
	1st	Cephalexin																							
		Cefazolin																							
		Cefoxitin																							
	2nd	Cefuroxime																							
S		Cefotetan																							
Cephalosporins		Cefdinir																							
dso		Cefixime																							
ha	3rd	Ceftriaxone																							
eb	,	Cefpodoxime																							
Ŭ		Ceftazidime																							
	4th	Cefepime																							
	_	Ceftaroline																							
	Sth	Ceftolozane																							
		Cefiderocol																							
Mono		Aztreonam																							
						tical R1 or R2 structures																			
		Blue Shaded						R1 or		truct	ures (	or coi	mpoe	nets	(ring	or bra	anch	chain	moie	ety)					
		Blank	No R	1 or F	R2 str	uctur	al sin	nilariti	es																

Adapted from Zagursky RJ et al. Allergy Clin Immunol Pract (2017)6: 72-81

## **Inpatient Management of COVID-19**

Scenario	Recommendation
Asymptomatic	Supportive care
Mild symptoms <sup>1</sup> , does not require O <sub>2</sub>	Paxlovid (nirmatrelvir + ritonavir) x 5 days <sup>2</sup>
	• If contraindication to Paxlovid <sup>3</sup> , Remdesivir x 3 days
Requires O <sub>2</sub> via NC	Remdesivir x 5 days <sup>4</sup>
	<ul> <li>If persistently ≥ 3-4L O<sub>2</sub> <u>add</u> dexamethasone</li> </ul>
	• If rapidly increasing $O_2 \ge 3-4L$ & systemic inflammation <sup>5</sup> add baricitinib <sup>6</sup> (preferred) or
	tocilizumab <sup>7</sup> if contraindication to baricitinib
Requires O <sub>2</sub> via high-flow or non-	Dexamethasone plus baricitinib <sup>6</sup> (preferred) or tocilizumab <sup>7</sup> if contraindication to baricitinib
invasive mechanical ventilation	May consider remdesivir x 5 day course for select patients <sup>4</sup>
	If started prior to progressing to high-flow or non-invasive mechanical ventilation
	Immunocompromised patients not started on remdesivir
Requires invasive mechanical ventilation	Dexamethasone plus baricitinib <sup>6</sup> (preferred) or tocilizumab <sup>7</sup> if contraindication to baricitinib
	• For patients who started on remdesivir and progressed to requiring mechanical ventilation, may
	consider continuing remdesivir to complete 5 day treatment course

Remdesivir, Paxlovid, molnupiravir, and baricitinib are ONLY orderable through the COVID-19 order menu for inpatient use

<sup>1</sup>Symptomatic COVID-19 infection is defined as the presence of one or more of the following:

 Fever, chills, cough, shortness of breath, fatigue, muscle aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting, diarrhea

<sup>2</sup>Paxlovid use beyond 5 days requires ID approval. Please page ID (443-5151) if a longer course is indicated

- eGFR > 60 mL/min: nirmatrelvir 300 mg with ritonavir 100 mg PO BID x 5 days
- eGFR 30 59 mL/min: nirmatrelvir 150 mg with ritonavir 100 mg PO BID x 5 days
- eGFR < 30 mL/min and iHD\*: nirmatrelvir 300 mg with ritonavir 100 mg PO on day 1, then nirmatrelvir 150 mg with ritonavir 100 mg PO daily x 4 days</li>
  - o iHD: when scheduled dose falls on a dialysis day, administer after dialysis

\*Dosing for patients with eGFR < 30 mL/min or iHD is not recommended according to the manufacturer; however, the risk of toxicity is likely to be minimal with a 5-day course of treatment. Recommendations are based on retrospective data in a limited number of patients.

<sup>3</sup>**Paxlovid** is contraindicated with drugs that are highly dependent on CYP3A for clearance. Many drug-drug interactions can be safely managed. However, some interactions cannot and may result in serious adverse reactions (ex. Amiodarone) or treatment failure with Paxlovid (ex. St John's Wort). The following resource can be utilized to assess for drug interactions <u>Liverpool COVID-19 Drug Interactions website</u>

<sup>4</sup>Remdesivir use longer than 5 days requires ID approval. Please page ID (443-5151) if a longer course is indicated

<sup>5</sup>Systemic Inflammation is defined as an elevation of  $\geq 1$  of the following: CRP, D-dimer, LDH, or ferritin

<sup>6</sup>Baricitinib should be continued for up to 14 days or until hospital discharge, whichever comes first. Patients should not receive both tocilizumab and baricitinib. Baricitinib must be approved by ID (443-5151). If patients have any of the following contraindications to baricitinib, consider using tocilizumab instead:

- eGFR < 15 mL/min or on renal replacement therapy (CRRT, HD, PD)
- Absolute neutrophil count < 500
- Platelets < 50,000 / mm3
- AST/ ALT exceeding 5 times the upper limit of normal
- Active tuberculosis (TB), bacterial, fungal, or viral infection aside from COVID-19

<sup>7</sup>**Tocilizumab** one time-dose may be considered for inpatients that do not qualify for baricitinib. Patients should not receive both tocilizumab and baricitinib. Tocilizumab must be approved by the ID (443-5151). Contraindications to tocilizumab include:

- History of or high risk for gastrointestinal perforation
- Absolute neutrophil count < 500
- Platelets < 50,000 / mm3
- AST/ ALT exceeding 5 times the upper limit of normal
- Active tuberculosis (TB), bacterial, fungal, or viral infection aside from COVID-19

## **Guidelines for Procalcitonin Use**

#### WHAT IS PROCALCITONIN

- Procalcitonin is a biomarker that has been used to aid in diagnosis of bacterial infection or sepsis
- May be used to guide antibiotic treatment decisions but should be used in conjunction with laboratory findings and should not overrule clinical judgement

#### INDICATIONS

# WHEN IS PROCALCITONIN RECOMMENDEDWHEN IS PROCALCITONIN NOT RECOMMENDEDDecision making about discontinuation of antimicrobials in:Severely immunocompromised (solid organ transplant patients, BMT<br/>patients, cancer patients receiving active treatment, HIV positive<br/>patients with CD4 <200, patients receiving immunosuppressive drugs<br/>other than prednisone)

#### HOW DO YOU USE PROCALCITONIN?

#### SUSPECTED RESPIRATORY INFECTION IN STABLE PATIENTS

- Not critically ill or high-risk (e.g., CAP PSI > IV / CURB 65 > 2, COPD GOLD > 111)
- Not severely immunocompromised (other than corticosteroids)
- No other concomitant infection requiring antibiotics



#### SUSPECTED SEPSIS IN CRITICALLY ILL PATIENTS

- Not severely immunocompromised (other than corticosteroids)
- Not on antibiotics for chronic bacterial infection (e.g., endocarditis, osteomyelitis)



#### LIMITATIONS

- Serum procalcitonin may be elevated due to non-infectious causes based on various patient factors
- The time course of bacterial infection and type of infectious process may impact the serum procalcitonin level

#### References

- 1. Samsudin, Intan, and Samuel D Vasikaran. "Clinical Utility and Measurement of Procalcitonin." The Clinical biochemist. Reviews vol. 38,2 (2017): 59-68.
- 2. Huang, David T et al. "Procalcitonin-Guided Use of Antibiotics for Lower Respiratory Tract Infection." The New England journal of medicine vol. 379,3 (2018): 236-249. doi:10.1056/NEJMoa1802670
- 3. Kamat, Ishan S et al. "Procalcitonin to Distinguish Viral From Bacterial Pneumonia: A Systematic Review and Meta-analysis." Clinical infectious diseases : an official publication of the Infectious Diseases Society of America vol. 70,3 (2020): 538-542. doi:10.1093/cid/ciz545
- 4. Daubin, Cédric et al. "Procalcitonin algorithm to guide initial antibiotic therapy in acute exacerbations of COPD admitted to the ICU: a randomized multicenter study." Intensive care medicine vol. 44,4 (2018): 428-437. doi:10.1007/s00134-018-5141-9

## AmpC β-Lactamases Mediated-Resistance

#### Background:

Production of  $\beta$ -lactamase is one of the main mechanisms of how microbes can confer beta-lactam antibiotic resistance. AmpC  $\beta$ -Lactamase-Producing Enterobacteriaceae are gram-negative bacteria which produce  $\beta$ -lactamases through induction of the AmpC pathway. When the AmpC gene is induced (expressed), susceptibility of beta-lactam antibiotics is limited.

Resistance mechanism of AmpC includes:

- Plasmid-mediated resistance (ex: Klebsiella pneumoniae, E. coli, Salmonella spp.)
- Non-inducible chromosomal resistance due to mutations (ex: E. coli, Shigella spp., Acinetobacter baumannii)
- Inducible resistance (ex: Enterobacter cloacae, Citrobacter freundii)

#### What makes inducible resistance different from other resistance mechanism?

Inducible resistance is species and antibiotic dependent. Certain bacterial isolates such as *Hafnia alvei, Enterobacter cloacae, Citrobacter freundii, Citrobacter youngae, Klebsiella aerogenes* (*Enterobacter aerogenes*), *Yersinia enterocolitica* (collectively known by acronym HECK-Yes) are well known to have AmpC inducible resistance. HECK-Yes isolates may initially test as susceptible to certain beta-lactam antibiotics and 3<sup>rd</sup> generation cephalosporins, however non-susceptibility to these agents may occur after treatment is initiated.

- Strong Inducers of AmpC: Aminopenicillins, 1<sup>st</sup> generation cephalosporins, cefoxitin, cefotetan
- Weak Inducers of AmpC: Piperacillin/tazobactam, aztreonam, 3<sup>rd</sup> generation cephalosporins (Ceftazidime, ceftriaxone, cefotaxime)

#### HECK-Yes and Empiric/Definitive Antibiotic Therapy:

Due to exposure of beta-lactams which can induce resistance in HECK-Yes isolates, IDSA recommends avoiding antibiotics known to be strong and weak inducers of AmpC in HECK-Yes pathogens including piperacillin/tazobactam, aztreonam, and 3<sup>rd</sup> generation cephalosporins (ceftriaxone, cefotaxime, ceftazidime).

	"HECK-Yes"									
	Hafnia alvei									
Enterobacter cloacae										
Citrobacter freundii or Citrobacter youngae										
Klebs	iella aerogenes (Enterobacter aerogenes)									
	Yersinia enterocolitica									
	Ertapenem									
Consider for Empiric/Definite	Cefepime (MIC ≤ 2)									
Antimicrobial Therapy	Fluroquinolones									
	Trimethoprim/Sulfamethoxazole									
	Aminopenicillins, 1 <sup>st</sup> generation cephalosporins, cefoxitin, cefotetan									
Avoid	Piperacillin/tazobactam									
	Aztreonam									
	3 <sup>rd</sup> generation cephalosporins (ceftriaxone, cefotaxime, ceftazidime)									

References:

<sup>1.</sup> Enterobacterales Bloodstream Infection Adult IV to PO Step-Down Guideline. Infectious Diseases Management Program at UCSF. https://idmp.ucsf.edu/content/enterobacteralesbloodstream-infection-adult-iv-po-step-down-guideline. Published 2022. Accessed April 9, 2022.

<sup>2.</sup> https://www.idstewardship.com/heck-yes-get-amped-updates-ampc-harboring-bacteria/. Published 2022. Accessed April 9, 2022.

<sup>3.</sup> Pranita T, Aitken S, Bonomo R, Mathers A, van Duin D, Clancy C. IDSA Guidance on the Treatment of Antimicrobial-Resistant Gram-Negative Infections: Version 2.0. Idsociety.org. https://www.idsociety.org/practice-guideline/amr-guidance-2.0/#. Published 2022. Accessed April 9, 2022.

## **Antibiotic Spectrum of Activity**

- Good activity = reliable coverage; often a good empiric drug option (depends on infectious etiology)
- Moderate activity = inconsistent coverage; may be treatment option in certain cases; confirm susceptibility
- Poor activity = Unreliable coverage; not a treatment option for this pathogen
- Enteric gram-negative rods = Escherichia Coli, Proteus spp., Klebsiella ssp.
- Anaerobes = GI: Bacteroides Fragilis; Oral: Peptostreptococci
- Atypicals = Legionella spp., Mycoplasma pneumoniae, Chlamydia pneumoniae

Antibiotic	Good Activity	Moderate Activity	Poor Activity
Penicillin	Most streptococci Anaerobes oral Treponema palladium	Enterococci	Everything else
Nafcillin	MSSA Streptococci		Everything else
Amoxicillin Ampicillin	Enterococci Streptococci Anaerobes oral	Enteric gram-negative rods Haemophilus	Everything else
Amoxicillin-clavulanate (Augmentin) Ampicillin-sulbactam (Unasyn)	Enterococci Streptococci Haemophilus Anaerobes GI and oral Enteric gram negative rods Acinetobacter (Unasyn)	MSSA	MRSA Pseudomonas ESBL and AmpC producers
Piperacillin- Tazobactam (Zosyn)	Pseudomonas Enterococci Streptococci Anaerobes GI and oral Enteric gram negative rods	MSSA	MRSA ESBL and AmpC producers
Cefazolin Cephalexin	MSSA Streptococci Anaerobes oral Enteric gram-negative rods (URINE ONLY)	Enteric gram-negative rods (outside of URINE)	MRSA Enterococci Pseudomonas ESBL and AmpC producers Anaerobes GI
Ceftriaxone Cefpodoxime	Streptococci Anaerobes oral Enteric gram-negative rods	MSSA	MRSA Enterococci Pseudomonas ESBL and AmpC producers Anaerobes GI
Cefepime	Pseudomonas Enteric gram-negatives Anaerobes oral	MSSA AmpC producers Acinetobacter	MRSA Enterococci ESBL producers Anaerobes GI
Ceftazidime	Pseudomonas Enteric gram-negative rods		Everything else
Ceftaroline	MSSA, MRSA Streptococci Anaerobes oral Enteric gram-negative rods	Enterococci	Pseudomonas Anaerobes GI ESBL and AmpC producers
Ertapenem	Enteric gram-negative rods ESBL producers MSSA Streptococci Anaerobes GI and oral	AmpC producers	MRSA Enterococci Pseudomonas

Antibiotic	Good Activity	Moderate Activity	Poor Activity
Meropenem	Pseudomonas	AmpC producers	MRSA
	Enteric gram-negative rods	Acinetobacter	
	ESBL producers	Enterococci	
	MSSA		
	Streptococci		
	Anaerobes GI and oral		
Aztreonam	Pseudomonas	Acinetobacter	Gram positive organisms
	Enteric gram negative rods		Anaerobes GI and oral
			ESBL and AmpC producers
Vancomycin	MRSA	M. tuberculosis (Linezolid)	Gram negative organisms
Dalbavancin	MSSA		Anaerobes GI
Daptomycin	Streptococci		
Linezolid	C. Difficle (Vancomycin PO)		
	Enterococci		
	Anaerobes oral		
Ciprofloxacin	Pseudomonas	MSSA	Anaerobes GI and oral
	Enteric gram negative rods		Streptococci
	ESBL and AmpC producers		Enterococci
Levofloxacin	Streptococci	MSSA	Enterococci
Moxifloxacin	Enteric gram negative rods		Anaerobes GI (Levo)
	ESBL and AmpC producers		Pseudomonas (Moxi)
	Pseudomonas (Levofloxacin)		
	Haemophilus		
	Anaerobes oral		
	Anaerobes GI (Moxifloxacin)		
Gentamicin	Enteric gram negative rods	Pseudomonas	Gram-positive organisms
Tobramycin	ESBL and AmpC producers	Enterococci (Gentamicin)	Anaerobes GI and oral
Amikacin			
Doxycycline	MRSA, MSSA	Streptococci	Enterococci
Minocycline	Atyipicals	Anaerobes oral	Anaerobes GI
		Enteric gram negative rods	Enteric gram negative rods
		(Minocycline)	(Doxycycline)
Azithromycin	Atypicals	Enteric gram-negative rods	Everything else
	H. Pylori	Streptococci	
		Anaerobes oral	
Metronidazole	Anaerobes GI	C. Difficle	Everything else
		H. Pylori	
Nitrofurantoin	Enteric gram-negative rods	Staphylococci spp.	Everything else
	ESBL producer	Enterococci	
Fosfomycin	E. Coli	Pseudomonas	Everything else
	ESBL E. Coli	Proteus and Klebsiella	
		Enterococci	
Sulfamethoxazole-	MSSA, MRSA	Strep Pnemoniae	Pseudomonas
trimethoprim (Bactrim)	Streptococci		Enterococci
	Enteric gram negative rods		Anaerobes GI and oral
	ESBL and AmpC producers		
	Stenotrophomonas		
	Pneumocystis jirovecii		
Clindamycin	Streptococci	MSSA, MRSA	Enterococci
		Anaerobes oral	Gram negatives
			Anaerobes GI
	ford Cuide Mob Editions Conford Cui		

Reference: Adapted from Sanford Guide Web Edition: Sanford Guide: Antibacterial Agents: Spectra of Activity

## **IV Antimicrobial Dosing**

- > Renal adjustments based on creatine clearance (mL/min) unless stated otherwise
  - For weight-based doses, use ideal body weight (IBW) unless...

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- $\circ$  ~ Total body weight (TBW) is less than IBW, use TBW
- TBW is > 120% of IBW, use adjusted body weight (adjBW)

Acyclovir	> 50	25-50	1	.0-25	< 10	)	iHD		CRRT		
Non-CNS HSV infections	5 mg/kg q8h	5 mg/kg q12h	5 mg	/kg q24h	2.5 mg q24ł	-	2.5 mg/kg x1 then qPN		5 mg/kg q24h		
<ul> <li>HSV meningitis</li> <li>VZV infections</li> </ul>	10 mg/kg q8h	10 mg/kg q12h		g/kg q24h	5 mg/kg	-	5 mg/kg x1 r then qPN	Л	10 mg/kg q12h		
Amikacin		Refer to "Aminogly	coside	dosing and	therapeuti	c monit	oring" on page	<u>s 42-43</u>			
Amphotericin B Liposomal				No renal do	-						
Fungal infections			-	ւց q24h (roւ			-				
Mold prophylaxis				ք q24h (roւ	und to near	est 25 r	ng)				
+Hydration &		00 mL IV pre- and				a sa al alta	<b>.</b>	25 50			
pre-medications	Give 1 hour prior to infusion: acetaminophen 500-650 mg PO/IV and diphenhydramine 25-50 mg PO/IV										
Ampicillin	> 50	10-50		< 1	10		iHD		CRRT		
<ul><li>Meningitis</li><li>Endovascular infection</li><li>Bone &amp; joint infection</li></ul>	2 gm q4h	2 gm q6l	h	1 gm	ı q8h	2	gm q12h	2	2 gm q6h		
Uncomplicated infection	2 gm q6h	1 gm q6l	h	1 gm	q12h	2	gm qPM	2	gm q8h		
Ampicillin-Sulbactam (Unasyn®)	≥ 30	15-30			15		iHD		CRRT		
Standard dose	3 gm q6h	3 gm q12	h	3 gm	q24h	3	gm q12h	(1) (1)	8 gm q6h		
Carbapenem-resistant Acinetobacter	3 gm q4h	3 gm q8l	h	3 gm	q12h	3	gm q12h	3 gm q4h			
Azithromycin	No renal dose adjustments										
Severe community-acquired pneumonia	500 mg q24h										
Non-severe community-acquired pneumonia		500 mg x1, then 250 mg q24h									
Aztreonam	> 50	31-50	1	.0-30	<10		iHD		CRRT		
Meningitis	2 gm q6h	2 gm q8h	2 gi	m q12h	1 gm q	12h					
UTI	1 gm q8h	1gm q8h	1 gi	m q12h	1 gm q	24h	2 gm x1 now,	then	2 gm q12h		
All other indications (incl. when combined with Avycaz®)	2 gm q8h	2 gm q8h	2 gi	m q12h	1 gm q	12h	qPM				
Cefazolin	> 30	10-29		<	10		iHD		CRRT		
- Uncomplicated SSTI - UTI	1 gm q8h	1 gm q12	h			_	x1 then 2 gm post HD	-			
All other indications	2 gm q8h	2 gm q12	h	1 gm q24h		or 2 gm/ 2 gm/ 3 gm post HD		2 gm q12h			
Surgical prophylaxis				ight < 120 k ight <u>&gt;</u> 120 k							
Cefepime	> 60	30-60	10-29 < 10		iHD		CRRT				
<ul> <li>Severe infections</li> <li>CNS</li> <li>Febrile Neutropenia</li> <li>Pseudomonas</li> </ul>	2 gm q8h	2 gm q12h	2 gi	m q24h 1 gm q24h		24h	1h 2 gm post H week		1 gm q8h		
Non-severe infections	2gm q12h	2 gm q24h	1 gi	m q24h	500 mg	q24h	1 gm on day	1, then			
Cystitis	1 gm q12h	1 gm q24h		mg q24h	500 mg (	500 mg		qPM bost HD	1 gm q8h		

Cefiderocol	>120	60-119	30-59	1	5-29	<15	ił	HD		CRRT			
All indications	2 gm q6h	2 gm q8h	1.5 gm q8h	1 gr	n q8h	750 mg q8h		) mg 12h	mg $\frac{<2L}{2.1-3}$		effluent rate: 1.5 gm q12h = 2 gm q12h = 1.5 gm q8h = 2 gm q8h		
Ceftaroline	> 50	31	-50	15-	15-30		5		iHD	)	CRRT		
Standard dose	600 mg q8		ng q8h	300 m	<b>U</b>	200 mg			200 mg	-	600 mg q12h		
SSTIs	600 mg q12		g q12h	300 m		200 mg	q12h	2	00 mg (		400 mg q12h		
Ceftazidime	> 50	31	-50	15-	·30	< 15	5		iHD		CRRT		
Standard dose	2 gm q8h	2 gm	q12h	2 gm	q24h	1 gm q	24h	-	gm IV x ind pos		2 gm IV q12h		
Ceftazidime-Avibactam (Avycaz®)	> 50	31-50	:	16-30	6-	-15	<u>&lt;</u> 5			iHD	CRRT		
Standard dose	2.5 gm q8h	1.25 gm c	xn	.94 gm q12h		4 gm 24h	0.94 gr q48h		0.94	gm qPM	2.5 gm q8h		
Ceftolozane-Tazobactam (Zerbaxa®)	>50	30	-50	15-	29	< 15	5		iHD	,	CRRT		
Standard dose	1.5 gm q8h 750 mg q8			375 m	g q8h	- No da	ita	the		ng q8h	No data		
Severe infection	3 gm q8h	m q8h	750 m	01				2.25 gm n 450 r	n x1, ng q8h				
Ceftriaxone				N	o renal d	ose adjustn	nent						
Mild infections (cystitis) and/or TBW < 50 kg		1 gm q24h											
Standard dose					2 g	m q24h							
Meningitis and Enterococcal endocarditis (synergy)					2 g	m q12h							
Ciprofloxacin	> 50		30-50			: 30		iHI	D		CRRT		
Standard dose		400 mg q12	h		400 n	ng q24h	-	~~					
<ul> <li>Pseudomonas</li> <li>Severe infection</li> </ul>	400 mg o	48h 4	100 mg q1	2h	400 n	ng q24h	4	00 mg	g qPM	400 mg q12h			
Clindamycin				N	o renal d	ose adjustn	nent						
Standard dose					600	) mg q8h							
Necrotizing SSTI, Group A streptococcus, or TBW > 120 kg					900	) mg q8h							
Colistin				No	renal d	ose adjustn	nent						
Standard dose		5 mg/kg x	1 loading	dose, the	n contac	t ID/ASP Ph	armacis	t for n	nainten	ance dose	2		
Dalbavancin		<u>&gt;</u> 30				< 30				iHC	)		
SSTI	-	1500 mg x1				)0 mg x1				1500 n	ng x1		
Severe Infection	1500 n	ng on day 1 ai	nd 8	1	000 mg	on day 1 an	d 8		150	00 mg on o	lay 1 and 8		
Daptomycin	≥	30		< 30			iHD				CRRT		
Mild to moderate infection	4-6 mg,	/kg q24h	4-(	6 mg/kg c	148h		mg/kg I` (evenin	ıg)		8-10	mg/kg q48h		
Severe infection	8-10 mg	/kg q24h	8-1	0 mg/kg	q48h	8-10	mg/kg l (evenin		h	6 m	ng/kg q24h		
Enterococcal infection	10 - 12 m	10 - 12 mg/kg q24h 10-12 mg/kg q48h				10-12	2 mg/kg (evenin		8h	6 m	ng/kg q24h		
Doxycycline Standard dose			No renal dose adjustment) 100 mg q12h										
Eravacycline	No rena	I dose adjusti	nent	Sev		atic impairr	nent		Str	rong CYP3A4 Inducer			
Standard dose		mg/kg q12h			1 mg/kg	q12 x2 dose mg/kg q24				1.5 mg/k			
	2	30		<30	ten I		iHD				CRRT		
Ertapenem				0 mg IV g24h 500 mg IV				then qPM D 3x week 1 gm IV q24h					
Fluconazole	> 50			10-50		< 10		iHD			CRRT		
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Oropharyngeal infection	100 mg q2	4h						-	x1 now, ost-HD	2	200 mg q24h		
Esophageal infection	200 mg q2	4h		% of target		6 of target	. 2	200 mg x1 now, then post-HD		2	100 mg q24h		
Systemic/ Severe infections	≤ 80 kg: 400 m 81-100 kg: 600 r > 100 kg: 800 m	ng q24h	- di	dose q24h		dose q24h -		400 mg x1 now, then post-HD			D-1200 mg per day, divided q12-24h		
Ganciclovir	> 70		50-69	2	5-49	10	-24	< 10 and iHD			CRRT		
CMV treatment	5 mg/kg q12h		mg/kg q12h	2.5 mg	/kg q24h		mg/kg 24h	we I	25 mg/kg 3x eekly (post HD if HD)		2.5-5 mg/kg q12-24h		
CMV prophylaxis	2.5 mg/kg q12h		g/kg q24	4n q	mg/kg 24h	q2	mg/kg 24h	We	25 mg/kg 3 eekly (post HD if HD)		No data		
Gentamicin		Refer to	"Amino	glycoside do	osing and t	herapeuti	c monito	ring" o	n <u>pages 42</u>	-43			
Imipenem-Cilastatin	> 60	3	30-60	1	5-30	<	15		iHD		CRRT		
- Standard dose - Nocardia	500 mg q6h		mg q6h		mg q8h		ernative ent	50	0 mg q12h		No data		
Nontuberculous mycobacteria	1 gm q12h	500	mg q12h	n 250 n	ng q12h								
Imipenem-Cilastatin- Relebactam (Recarbrio®)	> 90	60-9	-	30-60		5-30 < 1			iHD		CRRT		
Standard dose	1.25 gm q6h	1 gm q	6h	750 mg q6h	-	mg q6h No d		o data 500 mg q6h		No data			
Isavuconazole					o renal dos	-							
All indications					3h x 6 dose		72 mg q2						
Levofloxacin	> 50		20-	-		< 20		iHD			CRRT		
- UTI - Epididymitis	500 mg q24h		300 mg 250 mg		250 m	-		250 mg q48h		2	mg IV x1, then 50 mg q24h		
<ul> <li>Pseudomonas</li> <li>Other indications</li> </ul>	750 mg q24h	I	750 mg	g q48h	<u> </u>			750 mg x1, then 7 500 mg q48h			mg IV x1, then 00 mg q24h		
Linezolid				No	o renal dos	e adjustm	ient						
All indications		-				IV q12h							
Meropenem	> 50	2	26-50	10	0-25	<	10		iHD		CRRT		
- Standard dose - Pseudomonas	1 gm q8h	1 g	m q12h	500 n	ng q12h	500 m	g q24h	500 mg x1, then QPM			1 gm q8h		
- Meningitis - Acinetobacter	2 gm q8h	2 g	m q12h	1 gn	n q12h	1 gm	q24h	1 g	gm x1, then QPM		1 gm q8h		
Metronidazole	<u>≥</u>	10			< 10	)			iHD a	nd Cl	RRT		
Standard dose	500 n	ng q8h			500 mg	q12h			500				
Intra-abdominal infection				mg q12h				500 mg q12h					
C. difficile infection			500	mg q8h					500	mg q	8h		
Micafungin				No	o renal dos	-	ient						
Standard dose						g q24h				_			
Esophageal candidiasis Neutropenia Antifungal					150 m	g q24h							
Prophylaxis	50 mg or 100 mg q24h												
Minocycline	No renal dose adjustment												
Standard dose					ng once, th								
- Carbapenem-resistant -													
Acinetobacter	200 mg q12h												
- Stenotrophomonas maltophilia													
Nafcillin	No renal dose adjustment												
Meningitis and severe infections (ex: endocarditis)					2 gn	n q4h							
Uncomplicated infection					1 gm	n q6h							

Penicillin G	> 50		10-50	<	10	iHD		CRRT
<ul> <li>Neurosyphilis</li> <li>Meningitis</li> <li>Prosthetic Joint</li> </ul>	4 million units q4h	3 m	nillion units q4h	3 million	units q6h	2 million units	q6h	3 million units q4h
<ul><li>Endovascular</li><li>Bacteremia</li></ul>	3 million units q4h	3 m	nillion units q6h	2 million	units q6h	2 million units	q8h	3 million units q6h
Other indications	3 million units q6h	2 m	nillion units q6h	1 million	units q6h	2 million units o	12h	2 million units q6h
Piperacillin-Tazobactam (Zosyn®)	> 40		20-40	1	< 2	< 20 and iHD		CRRT
<ul> <li>Pseudomonas</li> <li>Severe infections</li> </ul>	4.5 gm q6h		4.5 gm c	l8h	4.	5 gm q12h		4.5 gm q8h
Standard dose	4.5 gm q8h		3.375 gm	q8h	4.	5 gm q12h		
Sepsis loading dose				4.5 gn	n once			
Remdesivir	No renal dose adjustment							
COVID-19 infection	200 mg x1, then 100 mg q24h							
Rifampin	No renal dose adjustment							
Mycobacterial infections				600 m	g q24h			
Prosthetic device infections				300 m	g q12h			
Endocarditis				300 m	ıg q8h	-		
Sulfamethoxazole-Trimethoprim (Bactrim <sup>®</sup> )*	> 30		15-30	<:	15	iHD		CRRT
- Systemic GNR infections	10 mg/kg/day	5	5 mg/kg/day	2.5 m	ng/kg	2.5-5 mg/kg x1	now	5-7.5 mg/kg/day
- Nocardia	divided q6-12h	di	vided q6-12h	q2		and qPM		divided q12h
- Pneumocystis pneumonia	15-20 mg/kg/day		-10 mg/kg/day	4-5 m		g/kg 5-10 mg/kg x1 i		10-15 mg/kg/day
- CNS infections	divided q6-12h		vided q12-24h	q2	4h	and qPM		divided q6-12h
*Note:	Calculated dose is based on <b>trimethoprim</b> component. IBW is preferred dosing weight. Use TBW if less than IBW and adjBW if TBW > 120% of IBW.							
Tigecycline	No renal dose adjustment Severe hepatic impairment					tic impairment		
Standard dose	100 mg x1, then 50 mg q12h 100 mg x1, then 25 mg q12h							
Tobramycin	Refer to "Aminoglycoside dosing and therapeutic monitoring" on pages 42-43							
Vancomycin	Refer to "Empiric vancomycin dosing and monitoring" on pages 44-45							
Voriconazole			<u>&gt; 50</u>					50
<ul> <li>All infections</li> </ul>	6 mg/kg q12h x 2 doses, then 4 mg/kg q12h Avoid: IV vehicle accumulates; consider PO							

# **PO Antimicrobial Dosing**

- Renal adjustments based on creatine clearance (mL/min) unless stated otherwise
- For weight-based doses, use ideal body weight (IBW) unless...
  - Total body weight (TBW) is less than IBW, use TBW
  - TBW is > 120% of IBW, use adjusted body weight (adjBW)

Acyclovir	<u>&gt;</u> 25	10-	-24	< 10	iHD	
Herpes simplex (HSV), initial episode	400 mg TID	200 m	ng TID	200 mg BID	200 mg BID	
HSV treatment, recurrent	400 mg TID	200		200 mg DID	200 mg DID	
immunosuppressed	400 mg mb 2		ng TID	200 mg BID	200 mg BID	
HSV treatment, recurrent	800 mg BID x 5 days					
immunocompetent	or 800 mg TID x 2	200 m	ng TID	200 mg BID	200 mg BID	
	days					
HSV suppression or prophylaxis	400 mg PO BID	200 m	-	200 mg BID	200 mg BID	
Herpes zoster treatment	800 mg PO 5 x daily	800 m	ng TID	400 mg BID	400 mg BID	
Varicella zoster (VZV) uncomplicated infection	800 mg PO 5 x daily	800 m	ng TID	400 mg BID	400 mg BID	
VZV prophylaxis, immunocompromised	800 mg BID or 200 mg 3 to 5 x daily	200 m	ng TID	200 mg BID	200 mg BID	
Amoxicillin	≥ 30	10-	-29	< 10	iHD	
Cystitis	500 mg TID	500 m	ng BID	500 mg daily	500 mg daily	
Prosthetic joint chronic suppression	1 gm TID or BID	500 m	ng BID	500 mg daily	500 mg daily	
All other infections	1 gm TID	1 gm	n BID	500 mg BID	500 mg BID	
Amoxicillin-Clavulanate (Augmentin <sup>®</sup> )	≥ 30	10-	-29	< 10	iHD	
All indications	875/125 mg BID	500/125	mg BID	500/125 mg daily	500/125 mg qPM	
Atovaquone	No renal dose adjustment					
<i>Pneumocystis jirovecii</i> pneumonia treatment	750 mg BID					
Pneumocystis jirovecii pneumonia						
prophylaxis	1500 mg daily					
Azithromycin		Dose (	no renal do	se adjustment)		
Non-severe pneumonia		500 mg	on day 1, th	nen 250 mg daily		
Severe pneumonia			500 mg	daily		
Cefpodoxime	≥ 30			< 30	iHD	
Standard dose	200 mg BID			200 mg daily	200 mg qPM	
Skin and soft tissue infection	400 mg BID			400 mg daily	200 mg qPM	
- Uncomplicated cystitis	100 mg BID			100 mg daily	100 mg qPM	
- Streptococcal pharyngitis	100 mg bib				100 mg qi wi	
Cefuroxime axetil	≥ 30	10-		< 10	iHD	
Standard dose	500 mg BID	250 m	-	250 mg daily	250 mg daily	
Cephalexin	≥ 30	15-	-29	< 15	iHD	
Standard dose	500 mg QID or 1,000 mg PO TID	500 m	ng BID	500 mg daily	500 mg qPM	
<ul> <li>Uncomplicated cystitis</li> <li>Streptococcal pharyngitis</li> </ul>	500 mg BID	250 m	ng BID	250 mg daily	250 mg qPM	
Ciprofloxacin	> 50	30-	-50	< 30	iHD	
Standard dose	500 mg	PO BID				
<ul><li>Pseudomonas infection</li><li>Blood stream infection</li></ul>	750 mg BID	500 m	ng BID	500 mg daily	500 mg QPM	

Clindamycin	No renal dose adjustment					
Standard dose			450 mg	-		
Skin and Soft Tissue infection (SSTI)	Weight-Based (using total body weight): 60 – 90kg: 300mg PO q8h 90 – 120kg: 450mg PO q8h 120 – 180kg: 450mg PO q6h >180 kg: 600mg PO q6h					
Dapsone		No	renal dose	adjustment		
Pneumocystis jirovecii pneumonia prophylaxis or treatment			100 mg	daily		
Doxycycline		No	renal dose	adjustment		
Standard dose			100 mg	; BID		
Post-exposure sexually transmitted infection prophylaxis (Doxy-PEP)	200	) mg PRN w	ithin 24-72	hr after condomless sex	(	
Ethambutol	>30			< 30	iHD	
Tuberculosis	15 mg/kg dai	ly	20-25	mg/kg 3 x weekly	20-25 mg/kg post-HD	
Fluconazole	> 50	10-	-50	< 10	iHD	
Oropharyngeal infection	100 mg daily				100 mg post-HD	
Esophageal infection	200 mg daily				200 mg post-HD	
Systemic/ Severe infection	<ul> <li>≤ 80 kg: 400 mg daily</li> <li>81-100 kg: 600 mg daily</li> <li>&gt; 100 kg: 800 mg daily</li> </ul>	50% of target dose daily		25% of target dose daily	400 mg post-HD	
Fosfomycin	> 50 < 50					
Uncomplicated cystitis, female			3 gm x1	dose		
Complicated cystitis	3 gm every 2	days x 3 dos	es	3 gm every 3 da	ays x 3 doses	
Isavuconazole		No	renal dose	adjustment		
All indications		372 mg PO (	q8h x 6 dose	es, then 372 mg daily		
Isoniazid		No	renal dose	adjustment		
Prevention of tuberculosis			300 mg	daily		
Treatment of tuberculosis	300 mg da	aily or 15 mg	g/kg TBW (u	p to 900 mg) 2-3 times	weekly	
Levofloxacin	> 50	20-	-49	< 20	iHD	
- UTI	500 mg daily	-	, then 250	500 mg x1, then 250	500 mg x1, then	
- Epididymitis	500 mg dany	mg o	daily	mg q48h	250 mg q48h	
- Pseudomonas	750 mg daily	750 m	g q48h	750 mg x1, then 500	750 mg x1, then	
- Other indications				mg q48h	500 mg q48h	
Linezolid				adjustment		
Tuberculosis		6	00 mg or 30			
All other indications			600 mg	•		
Metronidazole	> 10 < 10				iHD	
Standard dose	500 mg TID			500 mg BID	500 mg TID	
Intra-abdominal infection	500 mg BID 500 mg BID					
C. Difficle	500 mg TID 500 mg TID					
Minocycline	No renal dose adjustment					
Standard dose	200 mg once, then 100 mg q12h					
- Carbapenem-resistant -Acinetobacter - Stenotrophomonas maltophilia	- 200 mg q12h					
Molnupiravir (Lagevrio <sup>®</sup> )	No renal dose adjustment					
COVID-19 infection treatment	800 mg BID					
Moxifloxacin	No renal dose adjustment					
Standard dose			400 mg	daily		

Nirmatrelvir and Ritonavir (Paxlovid®)	eGFR > 60		eGFR 30 -59		eGFR < 30 and iHD				
		vir 300 mg	Nirmatrelvir 150 mg		Nirmatrel	+ Ritonavir 100 mg			
Mild to Moderate COVID-19 infection		ir 100 mg		-			Nirmatrelvir 150 mg + Ritonavir		
		D		ID	,	100 mg	-		
Nitrofurantoin	>	40		40-30			30 and iHD		
Cystitis treatment	100 m			100 mg BID					
	100 11		Safe for sh	nort term us	se, ≤7 days				
Oseltamivir	> 60	31-60	11-30	<u>&lt;</u> 10	iH	ID	CRRT		
Influenza treatment	75 mg	30 mg	30 mg	Avoid	30 mg p	oost-HD	75 mg BID		
	BID 75 mg	BID 30 mg	daily 30 mg	use Avoid	30 mg after every				
Influenza prophylaxis	daily	daily	q48h	use	other HE	•	30 mg daily		
Penicillin VK	Giung	aany			adjustment				
Standard dose				500 mg	-				
Cellulitis, long term suppression				250 to 500	-				
Posaconazole			No		adjustment				
Standard dose					, then 300 m				
Rifabutin		>	30			< 31	0		
Standard dose		300 m	g daily		150	mg daily if t	oxicity occurs		
Rifampin			No	renal dose	adjustment				
Mycobacterial infections				600 mg	daily				
Prosthetic device infections				300 mg	g BID				
Endocarditis	300 mg TID								
Sulfamethoxazole-Trimethoprim		30	15	-30		15	iHD		
(Bactrim®)*		50	1.5	-30	< 15				
UTI or prostatitis	1 DS t			tab BID	1/2 DS tab daily		1/2 DS tab qPM		
SSTI (Weight based dosing using total body weight)	60-9 1 DS tab 90-1: 2 DS tabs 120-1 2 DS tab >18	9 PO q8h 20kg: PO q12h	60-9 ½ DS tab 90-1: 1 DS tab 120-1 1 DS tab >18	90kg: 5 PO q8h 20kg: PO q12h 180kg: 5 PO q8h 0kg: 5 PO q6h	1 DS ta	ıb daily	1 DS tab qPM		
Pneumocystis jirovecii prophylaxis	or 3 x	b daily week	-		ily or 3 x we		1/2 DS tab qPM or 3 x week		
*DS = double s	trength (800	) mg sulfam							
Tedizolid			No		adjustment				
Standard dose				200 mg	-				
Valacyclovir	≥.	50	30	-50	10-29	< 10	iHD		
- HSV systemic infection - VZV treatment	1 grr	TID	1 gn	n BID	1 gm daily				
HSV genital, initial	1 gm BID			1 gm daily	500 mg	500 mg qPM			
HSV genital, recurrent	500 mg BID or 1 gm daily			500 mg daily	daily				
VZV prophylaxis	500 mg BID			500 mg daily					
Voriconazole	No renal dose adjustment								
Standard dose		6 mg/kg BID x 2 doses, then 4 mg/kg BID							

# Aminoglycoside Dosing and Therapeutic Drug Monitoring

High Dose Extended Interval Dosing Strategy (Preferred dosing strategy if no exclusions)

**Exclusions:** gram-positive synergy (e.g., enterococcal endocarditis), unstable renal function, burn, pregnant, or trauma patient



- Goal tobramycin/gentamicin trough of <1 mcg/mL</li>
- Goal amikacin trough of <4-8 mcg/mL

Repeat post-dose level if there are significant changes in renal function or volume status

### Barnes Jewish Nomogram: Amikacin 15 mg/kg



### Hartford Hospital Nomogram: Gentamicin/ Tobramycin 7 mg/kg



**Conventional Dosing Strategy** (Utilize if there is an exclusion to High Dose-Extended Interval Dosing)

- 1. Use IBW unless....
  - a. Patient weights less than IBW, use total body weight
  - b. Patient weighs > 120% IBW, use adjusted body weight
- 2. Calculate the initial dose

Tobramycin and gentamicin	1 - 2.5 mg/kg (round to nearest 20 mg)
Amikacin	5 - 7.5 mg/kg (round to nearest 125 mg)

3. Select a dosing interval based on the patient's creatinine clearance

Creatinine Clearance (mL/min)	Suggested Dosing Interval
> 60	Q8h
40-59	Q12h
20-39	Q24h
< 20	Dose by level

4. Once at steady state (~ 4<sup>th</sup> dose in patients with stable renal function), draw a trough level 30 min prior to the next infusion and a peak level 30 minutes after the infusion has ended.

Indication	Desired	Peak	Desired Trough	
	Gent/Tobra	Amikacin	Gent/Tobra	Amikacin
Pneumonia	8 - 10	25 – 35	< 1	< 4 – 8
Cellulitis, intra-abdominal, neutropenia, osteomyelitis, pyelonephritis	6 – 8	25 – 35	< 1	< 4 – 8
Cystitis or gram-positive synergy	3 – 5	20 – 25	< 1	< 4 – 8

- 5. Adjust the regimen as necessary and obtain repeat levels every 24 hours until at goal
  - a. Peak in range and trough elevated: extend the dosing interval
  - b. Peak above goal range and trough in range: decrease dose
  - c. Peak below goal range and trough in range: increase dose, possibly extend interval
- 6. Once peak and trough goals are achieved, order follow up trough level after 4<sup>th</sup> dose

# **Empiric Vancomycin Dosing**

#### Step 1: Determine vancomycin indication

Infection Type	Mild or Moderate	Severe (non-CNS)	CNS infection
AUC (mg*h/L)	400-500	500-600	N/A
Trough (mcg/mL)*	10-20	10-20	15-20
Peak (mcg/mL)^	30-40	30-40	N/A

\*Troughs < 10 may reduce antibiotic efficacy and > 20 may cause adverse reactions ^Target peak is an arbitrary number and does NOT represent therapeutic effectiveness

- Mild infections: cellulitis without systemic signs of infection, uncomplicated UTI
- Moderate infection: cellulitis with systemic signs of infection, complicated UTI
- Severe infection (Non-CNS): Pneumonia, bacteremia, endocarditis, sepsis, osteomyelitis
- CNS infections: Meningitis

Step 3: Calculate loading dose (consider in severe infections to attain therapeutic levels sooner)

- 20-35 mg/kg total body weight (TBW) if BMI 18.5 29 kg/m<sup>2</sup>
- 20-25 mg/kg TBW if BMI 
   <u>></u> 30 kg/m<sup>2</sup>
- Max 2000 mg per dose; round to nearest 250 mg increment

#### Step 4: Calculate maintenance dose

- 15 mg/kg TBW
- Max 2000 mg per dose; round to nearest 250 mg increment

Step 5: Determine maintenance dose administration frequency

• Contact team pharmacist and/or inpatient pharmacy for assistance with AUC target achievement

Estimated Creatinine Clearance (mL/min)	Dosing Interval to Consider
<u>≥</u> 100	q8h
80 - 99	q8h* or q12h
50 – 79	q12h
25-49	q24h
HD, PD, or CRRT	Contact pharmacist for assistance

### Vancomycin Monitoring



Prioritize trough range of 15-20 mcg/L as efficacy parameter in patients with CNS infections such as meningitis or patients with enterococcal endocarditis. Consider consulting the infectious diseases service for assistance in managing these patients.

# **HIV Antiretroviral Dosing**

Nucleoside/TIDE Reverse Transcriptase Inhibitors (N(t)RTIs)

Drug	Dosage Forms	Dose	Excretory Route	Dosage Adjustment in Renal Insufficiency and Hemodialysis
Abacavir (Ziagen <sup>a</sup> )	Tablet: 300 mg	300 mg PO BID	Hepatic and renal	No dosage adjustment in renal insufficiency
Note: Generic tablet is available	Oral solution: 20 mg/mL	or 600mg PO once daily		Child-Pugh ClassDoseA200mg PO BID (use oral soln)B or CContraindicated
Emtricitabine (Emtriva <sup>™</sup> )	Capsule: 200 mg Oral solution: 10mg/mL	200 mg PO once daily or 240mg (24 mL) oral soln once daily	Renal	CrCl (mL/min)         Capsule         Soln           30-49         200 mg q48h         120 mg q24h           15-29         200 mg q72h         80 mg q24h           <15
Lamivudine (Epivir®) Note: Generic products are available	Tablets: 100 mg, 150 mg, 300 mg Oral solution: 5 mg/mL, 10 mg/mL	150 mg PO BID or 300 mg PO once daily	Renal	CrCl (mL/min)         Dose           15-29         150 mg x1, then 100 mg q24h           5-14         150 mg x1, then 50 mg q24h           <5
Tenofovir Alafenamide (TAF) (Vemlidy <sup>®</sup> )	Tablet: 25mg	25 mg PO daily	Renal	CrCl (mL/min)       Dose         <15 and not on HD
Tenofovir disoproxil fumarate (TDF) (Viread <sup>®</sup> ) Note: Generic product is available	Tablets: 150 mg, 200 mg, 250 mg, 300 mg Oral powder: 40 mg/1 gm	300 mg PO once daily 7.5 level scoops of oral powder PO once daily (dosing scoop dispensed with each bottle; one level scoop contains 1 gm of oral powder)	Renal	CrCl (ml/min)Dose30-49300 mg q48h10-29300 mg BIW (i.e., q 72-96 hours)<10 not on HD
	- 0, 0	Mix oral powder with 2-4 ounces of soft food that does not require chewing. <b>Do not mix oral powder with liquid.</b>		

#### Nucleoside/TIDE reverse transcriptase inhibitors co-formulations

Drug	Dosage Forms	Dose	Excretory Route	Dosage Adjustment in Renal Insufficiency and Hemodialysis
Abacavir / Lamivudine	Tablet:	1 tablet once daily	Renal	Not recommended in patients with CrCl< 30 mL/min
(Epzicom <sup>®</sup> )	600 mg abacavir/			
	300 mg lamivudine			Child-Pugh Class Dose
				A Dose adjust Abacavir and use individual drugs
				B or C Contraindicated
Tenofovir alafenamide (TAF)/	Tablet:	1 tablet once daily	Renal	CrCl (mL/min) Dose
Emtricitabine	25 mg tenofovir AF/			< 30 and not on HD Not recommended
(Descovy <sup>®</sup> )	200 mg emtricitabine			< 30 and on HD 1 tablet once daily; take after HD on HD days
				Concomitant administration with: Rifamycins not recommended
Tenofovir disoproxil fumarate (TDF) /	Tablet:	1 tablet once daily	Renal	CrCl (mL/min) Dose
Emtricitabine	300 mg tenofovir DF/			30-49 1 tablet q48h
(Truvada <sup>®</sup> )	200 mg emtricitabine			< 30 or on HD Not recommended

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Drug	Dosage Forms	Dose	Excretory Route	Dosage Adjustment in Renal Insufficiency and Hemodialysis
Doravirine (Pifeltro <sup>ª</sup> )	Tablet: 100 mg	100 mg PO once daily	Hepatic	No dosage adjustment with renal impairment. Has not been studied in ESRD or on HD
				Child-Pugh ClassDoseA or BNo dosage adjustmentCNot studied
				Concomitant administration with:RifampinContraindicatedRifabutinDoravirine 100mg PO BIDRifapentineContraindicated
Efavirenz (Sustiva <sup>a</sup> )	Capsules: 50 mg, 200	600 mg PO once daily, at or before bedtime	Hepatic and renal	No dosage adjustment necessary in renal impairment. Caution with impaired hepatic function
<b>Note:</b> Generic product is available	mg Tablet: 600 mg		1 (110)	Concomitant administration with:         Rifampin       No dosage adjustment         Rifabutin       ↑ Rifabutin dose 450-600 mg per day         Rifapentine       No dosage adjustment

Etravirine	Tablets:	200 mg PO BID	Hepatic	No dose adjustment necessary in renal impairment
(Intelence <sup>a</sup> )	25 mg, 100 mg, 200mg	200 mg r 0 bib	riepatie	No dose adjustment necessary in renarmiparment
(intelence )	25 mg, 100 mg, 200 mg	Take following a meal		Child-Pugh Class Dose
		Take following a filear		A or B No dosage adjustment
				C No dose recommendation
				Concomitant administration with:
				Rifampin Do not co-administer
				Rifabutin Do not coadminister if with PI/r
				If without PI/r, use rifabutin 300mg once daily
				Rifapentine Do not co-administer
Nevirapine	Tablet: 200 mg	200 mg PO once daily for 2 weeks,	Hepatic and	On hemodialysis, an additional 200mg dose following each dialysis treatment
(Viramune <sup>â</sup> )		then 200 mg PO BID thereafter*	renal	is recommended
	Extended-release			
Note: Generic products are available	tablet: 400 mg	or		Child-Pugh Class Dose
				A No dosage adjustment
	Oral suspension:	400 mg XR once daily		B or C Contraindicated
	10 mg/mL			
				Concomitant administration with:
		*Repeat lead-in period if therapy is		Rifampin Do not co-administer
		discontinued for >7 days		Rifabutin No dosage adjustment
				Rifapentine Do not co-administer
Rilpivirine	Tablet: 25 mg	25 mg PO once daily	Hepatic	No dosage adjustment necessary in renal impairment
(Edurant <sup>â</sup> )				
				Child-Pugh Class Dose
				A or B No dosage adjustment
				C No dose recommendation
				Concernitent administration with
				Concomitant administration with: Rifampin Contraindicated
				Rifabutin ↑ Rilpivirine 50mg once daily
				Rifapentine Contraindicated

### Fixed-dose combinations containing NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR plus Two NRTIs

Drug	Dosage Forms	Dose	Excretory Route	Dosage Adjustment in Renal Insufficiency and Hemodialysis
Doravirine/	Tablet:	1 tablet once daily	Hepatic and renal	Not recommended if CrCl <50 mL/min
Lamivudine/	100 mg doravirine/			
Tenofovir DF	300 mg lamivudine/			Child-Pugh Class Dose
(Delstrigo <sup>â</sup> )	300 mg tenofovir DF			A or B No dosage adjustment
				C Not studied
Efavirenz/	Tablet:	1 tablet once daily	Hepatic and renal	Not recommended if CrCl <50 mL/min
Emtricitabine/	600 mg efavirenz/			
Tenofovir DF	200 mg emtricitabine/			Caution with impaired hepatic function
(Atripla <sup>â</sup> )	300 mg tenofovir DF			

Efavirenz/	Tablet:	1 tablet once daily on an empty	Hepatic and renal	Not recommended if CrCl <50 mL/min
Lamivudine/	600 mg efavirenz/	stomach, preferably at bedtime	-	
Tenofovir DF	300mg lamivudine/			Not recommended with moderate to severe hepatic impairment. Caution with mild hepatic
(Symfi <sup>â</sup> )	300 mg tenofovir DF			impairment
Efavirenz/	Tablet:	1 tablet once daily on an empty	Hepatic and renal	Not recommended if CrCl <50 mL/min or if on HD
Lamivudine/	400 mg efavirenz/	stomach, preferably at bedtime		
Tenofovir DF	300mg lamivudine/			Not recommended with moderate to severe hepatic impairment. Caution with mild hepatic
(Symfi Lo <sup>â</sup> )	300 mg tenofovir DF			impairment
Rilpivirine/	Tablet:	1 tablet once daily with a meal	Hepatic and renal	Not recommended CrCl <50 mL/min
Emtricitabine/	25 mg rilpivirine/			
Tenofovir DF	200 mg emtricitabine/			Child-Pugh Class Dose
(Complera <sup>a</sup> )	300 mg tenofovir DF			A or B No dosage adjustment
				C No dose recommendation
Rilpivirine/	Tablet:	1 tablet once daily with a meal	Hepatic and renal	Not recommended CrCl <30 mL/min who are not receiving chronic HD
Emtricitabine/	25 mg rilpivirine/			On Chronic HD: 1 tablet once daily. On HD days, take after dialysis
Tenofovir AF	200 mg emtricitabine/			
(Odefsey <sup>â</sup> )	25 mg tenofovir AF			Child-Pugh Class Dose
				A or B No dosage adjustment
				C No dose recommendation

#### **Protease Inhibitors**

Drug	Dosage Forms	Dose	Excretory Route	Dosage Adjustment in Renal Insufficiency and Hemodialysis
Atazanavir	Capsules:	ARV-naive:	Hepatic	ARV-naïve on HD: Atazanavir 300mg plus ritonavir 100mg once daily
(Reyataz <sup>â</sup> )	100mg, 150 mg,	Atazanavir 300mg plus ritonavir 100mg once		ARV-experienced on HD: ATV and ATV/ritonavir not recommended
	200 mg, 300 mg	daily		
				Child-Pugh Class Dose
	Pediatric powder:	or		A No dosage adjustment
	50 mg packet			B ATV 300mg unboosted for naive
		Atazanavir 400mg once daily		C Not recommended
		ARV-experienced: Atazanavir 300mg plus		Concomitant administration with:
		ritonavir 100mg once daily		Efavirenz Atazanavir 400 mg plus ritonavir 100 mg once daily
				Tenofovir DF Atazanavir 300 mg plus ritonavir 100mg once daily
Atazanavir/	Tablet:	One tablet once daily	Hepatic and	If used with Tenofovir DF:
Cobicistat	300mg co-formulated		renal	Not recommended if CrCl < 70mL/min
(Evotaz <sup>â</sup> )	with cobicistat 150 mg			Not recommended with hepatic impairment
				Concomitant administration with:
				Rifampin Contraindicated
				Rifabutin Do not co-administer
				Rifapentine Do not co-administer
Darunavir	Tablets: 75 mg, 150 mg,	ARV-naïve or no DRV mutations:	Hepatic	Mild to moderate hepatic impairment: No dose adjustment
(Prezista <sup>â</sup> )	600 mg, 800 mg	800 mg plus 100 mg RTV once daiy		
				Severe hepatic impairment: Not recommended

	Oral suspension:	ARV-experienced with one or more DRV		
	100 mg/mL	mutations: 600 mg plus 100 mg RTV twice daily		
Darunavir/	Tablet:	One tablet once daily	Hepatic and	If used with Tenofovir DF: Not recommended if CrCl < 70mL/min
Cobicistat	800 mg darunavir/	,	renal	
(Prezcobix <sup>â</sup> )	150 mg cobicistat	ARV-experienced with one or more DRV		Child-Pugh Class Dose
. ,	U U	mutations: Not recommended		A or B No dosage adjustment
				C Not recommended
				Concomitant administration with:
				Rifampin Contraindicated
				Rifabutin Do not co-administer
				Rifapentine Do not co-administer
Ritonavir	Capsule: 100 mg (soft	Primarily used for "boosting" and in	Hepatic	Refer to recommendations for the primary PI for hepatic dose adjustment
(Norvir <sup>â</sup> )	gelatin)	combination with other Pl's		
	Tablet: 100 mg	100 mg to 400 mg per day in 1 to 2 divided doses (refer to other PIs for specific dosing		
	Oral solution: 80 mg/mL	recommendations)		
	Oral powder: 100mg single packet			

Fixed-dose combinations containing PROTEASE INHIBITOR plus Two NRTIs

Drug	Dosage Forms	Dose	Excretory Route	Dosage Adjustment in Renal Insufficiency and Hemodialysis
Darunavir/	Tablet:	1 tablet once daily	Hepatic and	CrCl <30 mL/min – not recommended
Cobicistat/	800 mg darunavir/		renal	
Emtricitabine/	150 mg cobicistat/			On chronic HD: 1 tablet PO once daily. On HD days, administer after HD
Tenofovir AF	200 mg emtricitabine/			
(Symtuza <sup>®</sup> )	10 mg tenofovir AF			Not recommended in severe hepatic impairment

#### CHEMOKINE CO-RECEPTOR ANTAGONIST

Drug	Dosage Forms	Dose	Excretory Route	Dosage Adjustment in Renal Insufficiency and Hemodialysis
Maraviroc	Tablets:	Depends on presence of concomitantly administered medications:	Hepatic	No dosage recommendation with hepatic impairment. Maraviroc concentrations will likely
(Selzentry®)	150 mg, 300 mg	<ul> <li>150 mg BID with strong CYP3A inhibitors (with or without CYP3A inducers)including PIs (except TPV/r)</li> <li>300mg BID with NRTIs, T-20, TPV/r, NVP, and non-strong CYP3A inhibitors or inducers</li> <li>600mg BID with CYP3A inducers, including EFV, ETR, etc. (without a CYP3A inhibitor)</li> </ul>	and renal	be increased <u>CrCl &lt;30 mL/min or on HD:</u> <u>Without potent CYP3A4 inhibitors or inducers</u> : Maraviroc 300mg twice daily; if postural hypotension occurs, reduce to maraviroc 150 mg twice daily <u>With potent CYP3A4 inhibitors or inducers</u> : Not recommended

#### CD4 Post-attachment Inhibitor

Drug	Dosage Forms	Dose	Excretory Route	Dosage Adjustment in Renal Insufficiency and Hemodialysis
Ibalizumab	Single-dose 2-	Loading: A single dose of 2,000 mg diluted IV infusion over 30 minutes	Not well	No dosage recommendation in renal or
(Trogarzo <sup>®</sup> )	mL vial		defined	hepatic impairment
	containing 200 mg/1.33 mL	Maintenance: 800mg diluted IV infusion over 15 minutes OR IV push every 2 weeks		
	(150 mg/mL) of	Missed dose: If maintenance dose is missed by 3 days or more beyond scheduled dosing day, administer		
	ibalizumab	a loading dose of 2000 mg as soon as possible. Resume maintenance dose every 2 weeks thereafter		

#### gp-120-directed attachment inhibitor

Drug	Dosage Forms	Dose	Excretory Route	Dosage Adjustment in Renal Insufficiency and Hemodialysis	
Fostemsavir	Tablet: 600mg extended release	600mg PO BID	Hepatic and renal	No dosage adjustment required with renal impairment or those on HD	
(Rukobia <sup>®</sup> )				No dosage adjustment required with mild to severe hepatic impairment	
				Concomitant administration with:RifampinContraindicatedRifabutinWithout PI/r, no dosage adjustment With PI/s, use rifabutin 150mg PO once dailyRifapentineDo not co-administer	

#### Integrase Strand transfer INHIBITORs (INSTI)

Drug	Dosage Forms	Dose	Excretory Route	Dosage Adjustment in Renal Insufficiency and Hemodialysis
Bictegravir	Only available as a component of fixed-dose combination <b>BIKTARVY</b> <sup>a</sup>	BIKTARVY: One tablet PO once daily	Hepatic	Refer to BIKTARVY for details
Cabotegravir	Tablet: <b>(Vocabria<sup>â</sup>) =</b> 30 mg*	Vocabria	Hepatic	No dosage adjustment necessary for mild to moderate renal impairment
	*Must be obtained from manufacturer for oral lead-in and oral bridging during administration of Cabenuva (CAB IM/RPV IM)	30mg once daily		For severe renal impairment or on HD, increase monitoring for adverse events <u>Child-Pugh Class</u> <u>Dose</u> A or B       No dosage adjustment
	Long-acting injectable: Apretude <sup>a</sup> = individual product for IM long-	Apretude		C No recommendation
	acting pre-exposure prophylaxis (CAB IM)	Loading dose:		CAB PO and concomitant administration with:
	• 600-mg/3-mL vial	CAB 600mg/3mL IM monthly		Rifampin Contraindicated
		for 2 months		Rifabutin No dosage adjustment
	<b>Cabenuva</b> <sup>a</sup> (CAB IM and RPV IM) = co-packaged intra-muscular long-acting regimen	Continuation phase:		Rifapentine Contraindicated
	• 400-mg/2-ml vial or 600-mg/3-ml vial	CAB 600mg/3mL IM		CAB IM and concomitant administration with:
		q8 weeks		Rifampin Contraindicated
				Rifabutin Contraindicated
		See CABENUVA for dosing		Rifapentine Contraindicated
		information		

Dolutegravir (Tivicay <sup>â</sup> )	Tablet: 10 mg, 25 mg, 50 mg	ARV-naïve or treatment- experienced but integrase	Hepatic and renal	No dosage adjustment necessary with renal impairment.	
		strand inhibitor-naïve (INSTI-		Child-Pugh Class	Dose
	Tablet for suspension: 5 mg	<u>naïve):</u>		A or B	No dosage adjustment
		50 mg PO once daily		C	Not recommended
		INSTI-experienced with certain		ARV- or INSTI- na	aïve and concomitant administration with:
		known or clinically suspected		Rifampin	$\uparrow$ Dolutegravir 50 mg BID (only if no INSTI mutation)
		INSTI-resistance:		Rifabutin	No dosage adjustment
		50 mg PO BID		Rifapentine	Do not co-administer
Elvitegravir	Only available as a component of a fixed-dose	Genvoya <sup>â</sup>	Hepatic and	Concomitant administration with:	
	combination known as either	One tablet PO once daily	renal	Rifampin	Contraindicated
	Genvoya <sup>â</sup>			Rifabutin	Do not co-administer
	(elvitegravir/cobicistat/emtricitabine/TAF)	Stribild <sup>â</sup>		Rifapentine	Do not co-administer
	Stribild <sup>â</sup>	One tablet PO once daily			
	(elvitegravir/cobicistat/emtricitabine/TDF)				
Raltegravir	Tablet: 400 mg	Regular tablet: 400 mg PO BID	Hepatic	No dosage adjust	tment necessary in renal insufficiency.
(Isentress <sup>â</sup> )				No dosage adjustment with mild to moderate hepatic insufficiency No recommendation with severe hepatic insufficiency	
	Chewable tablets: 25 mg, 100 mg	High dose tablet: ARV-naïve or			
		ARV-experienced with virologic			
	Powder for oral suspension:	suppression on a regimen		Concomitant administration with:	
	100 mg single-use packet	containing RAL 400mg twice		Rifampin	*Raltegravir 800mg BID (*standard tablet only)
		daily: 1200 mg PO once daily		Rifabutin	No dosage adjustment
	High dose tablet: 600 mg			Rifapentine	Do not co-administer with once daily Rifapentine

#### Fixed-dose combinations containing INTEGRASE STRAND TRANSFER INHIBITOR plus One NRTI

Drug	Dosage Forms	Dose	Excretory Route	Dosage Adjustment in Renal Insufficiency and Hemodialysis
Dolutegravir/	Tablet:	1 tablet once daily with food	Hepatic	No dosage adjustment with renal insufficiency
Rilpivirine	50 mg dolutegravir/ 25 mg rilpivirine			Monitor for adverse effects when CrCl < 30 mL/min
(Juluca <sup>®</sup> )				
				Child-Pugh Class Dose
				A or B No dosage adjustment
				C No dose recommendation
				Concomitant administration with:
				Rifampin Contraindicated
				Rifabutin ↑ Rilpivirine 50 mg once daily
				Rifapentine Contraindicated

#### Fixed-dose combinations containing INTEGRASE STRAND TRANSFER INHIBITOR plus One NRTI

Drug	Dosage Forms	Dose	Excretory Route	Dosage Adjustment in Renal Insufficiency and Hemodialysis
Dolutegravir/	Tablet:	1 tablet once daily	Hepatic and	Not recommended if CrCl <30 mL/min
Lamivudine	50 mg dolutegravir/		renal	
(Dovato <sup>®</sup> )	300 mg lamivudine			Child-Pugh Class Dose
				A or B No dosage adjustment
				C No dose recommendation
				ARV- or INSTI- naïve and concomitant administration with:
				Rifampin $\uparrow$ Dolutegravir 50 mg BID (only if no INSTI mutation)
				Rifabutin No dosage adjustment
				Rifapentine Do not co-administer

#### Fixed-dose combinations containing INTEGRASE STRAND TRANSFER INHIBITORS plus Two NRTIS

Drug	Dosage Forms	Dose	Excretory Route	Dosage Adjustment in Renal Insufficiency and Hemodialysis
Bictegravir/	Tablet:	1 tablet once daily	Hepatic and	CrCl <30 mL/min – not recommended
Emtricitabine/	50 mg bictegravir/		renal	
Tenofovir AF	200 mg emtricitabine/			On chronic HD: 1 tablet PO once daily. On HD days, administer after HD
(Biktarvy <sup>â</sup> )	25 mg tenofovir AF			
				Child-Pugh Class Dose
				A or B No dosage adjustment
				C Not recommended
				Concomitant administration with:
				Rifampin Contraindicated
				Rifabutin Do not co-administer
				Rifapentine Do not co-administer
Elvitegravir/	Tablet:	1 tablet once daily	Hepatic and	CrCl <30 mL/min and not on chronic HD: Not recommended
cobicistat/	150 mg elvitegravir/		renal	
Emtricitabine/	150 mg cobicistat/			On chronic HD: 1 tablet PO once daily. On HD days, administer after HD
Tenofovir AF	200 mg emtricitabine/			
(Genvoya <sup>â</sup> )	10 mg tenofovir AF			No dosage adjustment necessary in mild-moderate hepatic impairment
				Not recommended in severe hepatic impairment
Elvitegravir/	Tablet:	1 tablet once daily	Hepatic and	Initial use not recommended with CrCl < 70 ml/min
cobicistat/	150 mg elvitegravir/		renal	<u>Continued</u> use not recommended with CrCl < 50 ml/min
Emtricitabine/	150 mg cobicistat/			
Tenofovir DF	200 mg emtricitabine/			No dosage adjustment necessary in mild-moderate hepatic impairment
(Stribild <sup>â</sup> )	300 mg tenofovir DF			Not recommended in severe hepatic impairment
Dolutegravir/	Tablet:	1 tablet once daily	Hepatic and	Not recommended CrCl <30 mL/min
Abacavir/	50 mg dolutegravir/		renal	Child-Pugh class A: dose adjust abacavir and use individual drugs
Lamivudine	600mg abacavir/			Contraindicated for Child-Pugh class B and C
(Triumeq <sup>â</sup> )	300 mg lamivudine			

#### LONG-ACTING INJECTABLE containing INTEGRASE STRAND TRANSFER INHIBITOR and NNRTI

Drug	Dosage Forms	Dose	Excretory Route	Dosage Adjustment in Renal Insufficiency and Hemodialysis
Cabotegravir	Available as part of the co-packaged	Monthly Dosing	Hepatic	No dosage adjustment necessary for mild to moderate renal impairment
IM/ Rilpivirine	intramuscular long-acting regimen (CAB	Loading dose: CAB 600mg/3mL IM x 1 dose and RPV		
IM	IM and RPV IM)	900mg/3 mL IM x 1 dose		For severe renal impairment or on HD, increase monitoring for adverse
(Cabenuva <sup>â</sup> )				events
	(CABENUVA <sup>â</sup> )	Continuation phase: CAB 400mg/2mL IM and		
	600 mg/900 mg kit contains:	RPV 600mg/2mL every 4 weeks		Child-Pugh Class Dose
	CAB 600 mg/3 mL vial and			A or B No dosage adjustment
	RPV 900 mg/3 mL vial	Every 2-month Dosing		C No dose recommendation
		Loading dose: CAB 600mg/3mL IM monthly and RPV		
	(CABENUVA <sup>â</sup> )	900mg/3 mL IM monthly for 2 doses		Concomitant administration with:
	400 mg/600 mg kit contains:			Rifampin Contraindicated
	CAB 400 mg/2 mL vial and	Continuation phase: CAB 600mg/3mL IM and RPV		Rifabutin Contraindicated
	RPV 600 mg/2 mL vial	900mg/3mL every 8 weeks		Rifapentine Contraindicated

#### **CAPSID INHIBITOR**

Drug	Dosage Forms	Dose	Excretory Route	Dosage Adjustment in Renal Insufficiency and Hemodialysis
Lenacapavir (Sulenca <sup>â</sup> )	Tablets: 300 mg Injection in a dosing kit containing: 2 single-dose vials each containing 463.5 mg/1.5 ml (309mg/mL) of lenacapavir	Initiation with one of two options followed by once every 6-months maintenance dosing.Initiation Option 1Day 1927 mg by SQ injections and 600mg orallyDay 2600mg orallyInitiation Option 2Day 1600mg orallyDay 2Day 2600mg orallyDay 2600mg orallyDay 2600mg orallyDay 2600mg orallyDay 3300mg orallyDay 4927 mg SQ injectionsMaintenance927 mg SQ injections every 6 months (26 weeks) from the date of the last injection +/- 2 weeksMissed dose: If more than 28 weeks since last injection, then restart initiation from Day 1 using either Option 1 or Option 2	Hepatic	No dosage adjustment required with renal impairment. Lenacapavir has not been studied in patients with ESDR (estimated creatinine clearance less than 15 mL per minute). No dosage adjustment required with mild or moderate hepatic impairment. Lenacapavir has not been studied in patients with severe hepatic impairment. <u>Concomitant administration with</u> : Rifampin Contraindicated Rifabutin Do not co-administer Rifapentine Do not co-administer