TREATMENT GUIDELINE FOR ADULT PATIENTS WITH BLOODSTREAM INFECTIONS

Purpose:
This guideline is intended to help guide antimicrobial therapy for patients admitted to adult service lines following the results of Gram Stain, Organism Identification (with or without Verigene™ molecular resistance results), and Antimicrobial Susceptibilities. Deviation from the recommendations in this guideline may be required for patients with concomitant infections, history of resistant pathogens, or with antimicrobial allergies or intolerance.

The recommendations in this guideline reflect susceptibility patterns found at Michigan Medicine.

How to use this guideline:
For patients with ONLY Gram stain results, refer to the left column (labeled GRAM STAIN) for treatment recommendations.

For patients with organism identification results, refer to the middle column (labeled ORGANISM IDENTIFICATION) for treatment recommendations.

For patients with antimicrobial susceptibility results, refer to the right column (labeled SUSCEPTIBILITIES) for treatment recommendations.

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10/21: revised gram-negative section

The recommendations in this guide are meant ot serve as treatment guidelines for use at Michigan Medicine facilities. If you are an individual experience a medical emergency, call 911 immediately. These guidelines should not replace a provider’s profession medical advice based on clinical judgment, or be used in lieu of an Infectious Diseases consultation when necessary. As a result of ongoing research, practice guidelines may from time to time change. The authors of these guidelines have made all attempts to ensure the accuracy based on current information, however, due to ongoing research, users of these guidelines are strongly encouraged to confirm the information contained within them through and independent source.

If obtained from a source other than med.umich.edu/asp, please visit the webpage for the most up-to-date document.
**Gram Stain**

**Organism Identification**

**Yeast:**
- Micafungin
- Consult ID

If suspicion for *Cryptococcus* or *Histoplasma* (fungemia in setting of pneumonia or meningitis in immunocompromised patient), call Infectious Diseases consult service for immediate antifungal recommendations.

**All Candida species:**
- Continue Micafungin

See Candidemia Guideline. Therapy should not be de-escalated until guideline criteria are met.

ID consult is strongly recommended.

If concern for urinary, ocular, endocarditis, or CNS infection, alternative therapy may be needed.

Consult with ID.

**Cryptococcus spp.:**
- Liposomal amphotericin B (Ambisome™)
- Flucytosine

Consult ID

**Histoplasma:**
- Liposomal amphotericin B (Ambisome™)

Consult ID

**Susceptibilities**

- *C. albicans, C. parapsilosis, C. tropicalis, C. dublinensis,* and *C. lusitaniae:*
  - Consider de-escalation to Fluconazole for clinically stable patients with clearance of blood cultures and fluconazole susceptibility.
  - Otherwise: Micafungin

See Candidemia Guideline. Therapy should not be de-escalated until guideline criteria are met, in conjunction with ID consult recommendations.

- *C. glabrata* with fluconazole MIC ≤ 8 (SDD):
  - Consider de-escalation to Fluconazole for clinically stable patients with clearance of blood cultures
  - Otherwise: Micafungin

**Cryptococcus spp.:**
- Fluconazole may be appropriate for step down therapy when criteria is met in conjunction with ID consult recommendations

**Histoplasma:**
- Step down therapy may be appropriate when clinically stable in conjunction with ID consult recommendations
GRAM STAIN

*Gram-positive cocci in clusters: Vancomycin

ORGANISM IDENTIFICATION

S. aureus and mecA negative:
- Endocarditis or CNS infection: Oxacillin
- Other infections: Cefazolin

S. aureus and mecA positive or mecA not performed:
- Vancomycin

S. lugdunensis:
- Vancomycin
- Consult ID

Consider discontinuing adjunctive gram-negative therapy between 48-72 hours if cultures are negative for gram-negative pathogens, except for patients with intra-abdominal infections

Single positive culture for Coagulase-negative Staphylococcus or S. epidermidis in suspected infection of prosthetic material, neutropenia, or in hemodynamically unstable patients:

S. epidermidis and mecA negative:
- Cefazolin

S. epidermidis and mecA positive or coagulase negative
- Staphylococcus: Vancomycin

For patients who do not meet the above criteria, a single positive culture for coagulase-negative Staphylococcus or S. epidermidis may represent contamination, assess for possible source of infection and hold antibiotics if clinically stable

Susceptibilities

S. aureus or S. lugdunensis sensitive to methicillin:
- Non-CNS/endocarditis: Cefazolin
- CNS infection or endocarditis: Oxacillin
- Life-threatening PCN allergy: Vancomycin

S. aureus or S. lugdunensis intermediate or resistant to methicillin:
- Vancomycin

Antibiotic susceptibilities are only performed when coagulase-negative Staphylococcus or S. epidermidis grow from 2 or more bottles.

If growth from 1 blood culture bottle, assess for possible source of infection, repeat blood cultures, and hold antibiotics if clinically stable

Coagulase-negative Staphylococcus or S. epidermidis sensitive to methicillin:
- Non-CNS/endocarditis: Cefazolin
- CNS infection or endocarditis: Oxacillin
- Life-threatening PCN allergy: Vancomycin

Coagulase-negative Staphylococcus or S. epidermidis intermediate or resistant to methicillin:
- Vancomycin
Gram Stain

Gram-positive cocci in chains or pairs:
Vancomycin

Heme-onc, SICU, solid organ transplant:
Linezolid

BMT with ANC ≥ 1,000:
Linezolid

BMT with ANC < 1,000:
Daptomycin

Organism Identification

E. faecalis and vanA/vanB Negative:
Ampicillin
(consider piperacillin-tazobactam as alternative for intra-abdominal infections)
Life-threatening PCN allergy: Vancomycin

E. faecalis and vanA/vanB positive:
Ampicillin
(consider piperacillin-tazobactam as alternative for intra-abdominal infections)
Life-threatening PCN allergy: Linezolid or Daptomycin for BMT patients with ANC < 1,000

E. faecium and vanA/vanB negative:
Vancomycin

E. faecium and vanA/vanB positive:
Linezolid or Daptomycin for BMT patients with ANC < 1,000

E. casseliflavus, E. gallinarium:
Linezolid or Daptomycin for BMT patients with ANC < 1,000

Other Enterococcus species:
Vancomycin

S. pneumoniae, S. anginosus or Streptococcus species:
Penicillin or Ampicillin
Non-CNS/endocarditis: Ceftriaxone
CNS infection or endocarditis: Ceftriaxone + Vancomycin
Febrile neutropenia: Vancomycin + anti-Pseudomonal beta-lactam

S. agalactiae or S. pyogenes:
Penicillin or Ampicillin
Mild PCN allergy: Cefazolin (if no CNS infection)
Life-threatening PCN allergy: Vancomycin

Susceptibilities

Penicillin-based antibiotics should be first line therapy for all Enterococcus species if sensitive:

Ampicillin
(consider ampicillin-sulbactam or piperacillin-tazobactam for intra-abdominal infections)

Life-threatening PCN allergy or ampicillin-resistant Enterococcus:
Vancomycin

Patients with vancomycin allergy or ampicillin and vancomycin-resistant Enterococcus:
Linezolid or Daptomycin for BMT patients with ANC < 1,000

Patients with suspected endocarditis will likely require combination therapy and ID consult is strongly recommended

Penicillin-based antibiotics should be first line therapy for all Streptococcus species infections, if sensitive:

Penicillin or Ampicillin
Mild PCN allergy: Cefazolin (if no CNS infection)
Mild PCN allergy CNS infection: Ceftriaxone
Life-threatening PCN allergy: Vancomycin

Febrile neutropenic patients should be continued on anti-Pseudomonal beta-lactam
GRAM STAIN

*Gram-negative bacilli: Piperacillin-tazobactam or Cefepime (add metronidazole for intra-abdominal infections)

*Evaluate if patient has history of resistance to piperacillin-tazobactam or cefepime with prior year and modify therapy accordingly

ORGANISM IDENTIFICATION

E. coli, Klebsiella, Proteus, Serratia, Morganella:
No CTX-M, KPC, IMP, VIM, NDM, OXA detected:
Cefepime or Piperacillin-tazobactam

CTX-M positive:
Meropenem

KPC positive:
Meropenem-vaborbactam

IMP, VIM, or NDM positive:
Ceftazidime-avibactam + Aztreonam or Cefiderocol

OXA positive:
Ceftazidime-avibactam

Enterobacter cloacae, Citrobacter freundii, or Klebsiella aerogenes:
No CTX-M, KPC, IMP, VIM, NDM, OXA detected:
Cefepime

CTX-M positive:
High-dose Meropenem

KPC positive:
Meropenem-vaborbactam

IMP, VIM, or NDM positive:
Ceftazidime-avibactam + Aztreonam or Cefiderocol

OXA positive:
Ceftazidime-avibactam

SUSCEPTIBILITIES

Narrow antibiotic selection based on susceptibility results, clinical status, concomitant infections:

- Narrow-spectrum antibiotics are preferred if no resistance or allergies. These include ampicillin, penicillin, ampicillin-sulbactam, cefazolin, and cefuroxime.
- ID consult is strongly encouraged for patients with infections from organisms with KPC, IMP, VIM, NDM, or OXA resistance genes

Enterobacter cloacae, Citrobacter freundii, and Klebsiella aerogenes frequently have an inducible beta-lactamase resistance gene (AmpC), which can confer resistance to penicillin, ampicillin, ampicillin/sulbactam, and 1st-3rd generation cephalosporins. Cefepime should be first-line therapy if susceptible.

Citrobacter koseri is not associated with having AmpC gene, and narrow spectrum antibiotics should be prescribed if susceptible.
**GRAM STAIN**

- *Gram-negative bacilli:
  - Piperacillin-tazobactam
  - Cefepime

  (add metronidazole for intra-abdominal infections)

*Evaluate if patient has history of resistance to cefepime with prior year and modify therapy accordingly

**ORGANISM IDENTIFICATION**

*Pseudomonas aeruginosa*

- **No CTX-M, KPC, IMP, VIM, NDM, OXA detected:**
  - **Cefepime** or **Piperacillin-tazobactam**. Consider empiric double coverage with tobramycin

- **IMP, VIM, or NDM positive:**
  - **Cefiderocol + tobramycin** until susceptibilities result

- **CTX-M, KPC, OXA positive:**
  - Contact ID – unusual genotype

*Acinetobacter baumanii*

- **No IMP, VIM, NDM, OXA detected:**
  - High-dose **Meropenem + minocycline** until susceptibilities result

- **OXA, IMP, VIM, or NDM positive:**
  - **Cefiderocol + minocycline** until susceptibilities result

- **CTX-M or KPC positive:**
  - Contact ID – unusual genotype

**SUSCEPTIBILITIES**

Narrow antibiotic selection based on susceptibility results, clinical status, concomitant infections.

- If Pseudomonas isolate is resistant to cefepime, piperacillin-tazobactam, meropenem, imipenem, aztreonam, levofloxacin and ciprofloxacin, request *ceftolozane-tazobactam, ceftazidime-avibactam*, and *meropenem-vaborbactam* susceptibilities from microbiology lab (phone number 6-6831)

- Double coverage of Pseudomonas is not indicated after susceptibilities are available, unless isolate is resistant to all beta-lactam antibiotics, cystic fibrosis patient, or decompensating on susceptible antibiotics

Narrow antibiotic selection based on susceptibility results, clinical status, concomitant infections.

- There is no evidence double coverage of Acinetobacter improves outcomes. The decision to double cover should be made based on source of bacteremia, severity of infection, and patient’s medical history.
**GRAM STAIN**

*Gram-negative bacilli:*
- Piperacillin-tazobactam or Cefepime
  (add metronidazole for intra-abdominal infections)

*Evaluate if patient has history of resistance to cefepime with prior year and modify therapy accordingly

**Gram-positive rod:**
- Most likely the result of skin flora contamination of blood culture
- Consider treatment in HD unstable, prosthetic material with suspected infection, BMT, Neutropenia: Vancomycin
- If concern for Listeria: Ampicillin

**ORGANISM IDENTIFICATION**

**Achromobacter:**
- Piperacillin-tazobactam
  (Life-threatening PCN allergy: Meropenem)
  (Avoid cefepime unless susceptibility is verified)

**Stenotrophomonas:**
- Trimethoprim-sulfamethoxazole
  (Sulfa-allergy: Levofloxacin + minocycline)
  (Piperacillin-tazobactam and cefepime do not have activity against Stenotrophomonas)

**Susceptibilities**

Narrow antibiotic selection based on susceptibility results, clinical status, concomitant infections.

- Achromobacter is frequently multi-drug resistant, and ID consult is encouraged to guide appropriate management of these infections
- Trimethoprim-sulfamethoxazole should be dosed 10 mg/kg/day in 2-4 divided doses for patients with good renal function when treating *Stenotrophomonas* bacteremia

**Bacillus, Lactobacillus, and Corynebacterium** spp. are possible contaminants, consider treatment in HD unstable, prosthetic material with suspected infection, BMT, solid organ transplant, neutropenia

- **Bacillus or Corynebacterium** spp.: Vancomycin
- **Lactobacillus:** Piperacillin-tazobactam
- **Listeria:** Ampicillin

Patients with multiple positive sets of blood cultures are more likely true infection. Consider ID consult.

**SUSCEPTIBILITIES**

Narrow antibiotic selection based on susceptibility results, clinical status, concomitant infections.

- Susceptibilities will not be routinely performed by the microbiology lab. Please call to request susceptibilities if strong suspicion for infection