Sepsis: Empiric Antibiotic Selection Pathway

Early initiation of appropriate therapy is associated with improved outcomes in severe sepsis and septic shock and these guidelines are intended for use in patients with these syndromes only. All patients with suspected sepsis should have appropriate cultures obtained, although antimicrobial therapy should not be unduly delayed for this. Delays in initiating active therapy have been associated with worsened clinical outcomes and so antimicrobials should be initiated as rapidly as possible. The addition of a second antimicrobial agent can expand the empiric coverage for resistant Gram-negative pathogens. This combination therapy has been advocated by international consensus guidelines (Surviving Sepsis Campaign) in critically ill patients in severe sepsis or septic shock given delays to active therapy in this population has been associated with an increased mortality. Despite the clear mortality benefit of initially active therapy in critically ill patients, combination therapy remains controversial. The addition of a second agent has not been definitively associated with improved outcomes and depending on the severity of illness and patient population may be associated with worsened outcomes. Therefore, the addition of a second agent (e.g. tobramycin added to anti-pseudomonal beta-lactam) should be based on patient severity of illness, the likelihood of isolating resistant Gram-negative pathogens, and the potential adverse effects of additional therapy. Antibiotic therapy should be narrowed to target the isolated pathogen when culture results become available. Patients who have milder forms of infection may be more appropriately treated with narrow spectrum agents and antibiotic choices in these patients should be based upon current guidelines and clinical judgment. De-escalation to a single active agent is **strongly** recommended when culture and susceptibility results return.

EIAD: extended interval aminoglycoside dosing panel
+/- denotes that the drug is optional and use should be based on assessment of severity of infection and likelihood of resistance or isolation of the pathogen the agent targets

Suspected Source of Infection	Suggested Antibiotics
Unknown (includes catheter related blood stream infection) ‡	Vancomycin IV per pharmacy consult (initial 25mg/kg loading dose) **PLUS EITHER** Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours **OR** Cefepime 1 gm IV q6hr **+/-** Tobramycin 7 mg/kg IV EIAD Severe beta-lactam allergy (anaphylaxis, hives): Vancomycin IV per pharmacy consult (initial 25mg/kg loading dose) **PLUS** Aztreonam 2 gm IV q8h **+/-** Tobramycin 7 mg/kg IV EIAD ‡Consider Micafungin 100mg IV qday in patients at high risk for invasive candidiasis. Major risk factors predicting candidemia at TNMC include: 1) Broad-spectrum antibiotics, 2) Central venous catheter, 3) Receipt of TPN, 4) Abdominal surgery, and 5) Steroid use. Presence of 2 or fewer of the risk factors suggests a 99.4% chance of **not** developing candidemia, while patients with >2 risk factors have a 4.7% risk of developing candidemia. See Institutional Guidelines for the Treatment of Invasive Candidiasis for further information.
Intra-abdominal Source	Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours **OR** Cefepime 1g q6h hours **PLUS** Metronidazole 500 mg IV q8h **+/-** Gentamicin **OR** Tobramycin 7 mg/kg IV EIAD **+/-** Vancomycin per pharmacy consult (initial 25mg/kg loading dose)

	<u>Severe beta-lactam allergy (anaphylaxis, hives):</u> Vancomycin per pharmacy consult (initial 25mg/kg loading dose) **PLUS** Aztreonam 2gm IV q8h **PLUS** Metronidazole 500 mg IV q8h **+/-** Gentamicin **OR** Tobramycin 7 mg/kg IV EIAD
Urinary Tract **Patients should be assessed for risk of multi-drug resistant pathogens.** Suggested risk factors for resistant pathogens: 1) Residence in long-term care facility (LTCF) 2) Recent receipt of broad spectrum antibiotics 3) History of MDR urinary pathogen 4) History of recurrent UTI 5) Nosocomial UTI	**Not at risk for multi-drug resistant organisms** Ceftriaxone 1g IV q24h (2 grams if >80kg) **+/-** Gentamicin 7 mg/kg EIAD <u>Severe beta-lactam allergy (anaphylaxis, hives):</u> Aztreonam 2 gm IV q8hr **+/-** Gentamicin 7 mg/kg IV EIAD **At risk for multi-drug resistant organisms** Cefepime 1 gm IV q6hr **OR** Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours **+/-** Gentamicin 7 mg/kg IV EIAD **+/-** Vancomycin per pharmacy consult (initial 25mg/kg loading dose) <u>Severe beta-lactam allergy (anaphylaxis, hives):</u> Aztreonam 2 gm IV q8h **PLUS** Gentamicin 7 mg/kg IV EIAD **PLUS** Vancomycin per pharmacy consult (initial 25mg/kg loading dose)
Community Acquired Pneumonia – No Pseudomonas Risk Factors Excludes nursing home patients. See clinical pathways for pneumonia at www.nebraskamed.com/asp	Ceftriaxone 1 gram (2 grams if > 80 kg) IV q24h **PLUS EITHER** Levofloxacin 750 mg IV q24h **OR** Azithromycin 500 mg IV q24h <u>Severe beta-lactam allergy (anaphylaxis, hives):</u> Levofloxacin 750 mg IV q24h **+/-** Vancomycin IV per pharmacy consult (initial 25mg/kg loading dose) **+/-** Aztreonam 2 gm IV q8h
Community Acquired Pneumonia – Pseudomonas Risk Factors (structural lung disease, >10mg prednisone/day, malnutrition) **Excludes nursing home patients.**	Cefepime 1 gm IV q6hr **OR** Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours **PLUS** Azithromycin 500 mg IV q24h **+/-** Tobramycin 7 mg/kg IV EIAD

See clinical pathways for pneumonia at www.nebraskamed.com/asp	<u>Severe beta-lactam allergy (anaphylaxis, hives):</u> Levofloxacin 750 mg IV q24h **PLUS** Aztreonam 2 g IV q8h **+/-** Tobramycin 7 mg/kg IV EIAD
Nosocomial Pneumonia: healthcare-associated pneumonia (HCAP), hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP) **Classification as healthcare-associated pneumonia:** • Antimicrobial therapy in preceding 90 d • Hospitalization for >**2d** in preceding 90 d • Residence in a nursing home or extended care facility • Home wound care • Home infusion therapy (including antibiotics) • Chronic dialysis within 30 d • Immunosuppressive disease and/or therapy See clinical pathways at www.nebraskamed.com/asp **Add azithromycin if requiring coverage of atypical pathogens (e.g. *Legionella sp*.) Do not combine with levofloxacin.** **In patients with beta-lactam allergy add levofloxacin if suspicion for *S. pneumoniae* infection and/or clindamycin if concern for aspiration pneumonia/anaerobes**	Vancomycin IV per pharmacy consult (initial 25mg/kg loading dose) (Linezolid is also an option) **PLUS** Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours **OR** Cefepime 1 gm IV q6hr **+/-** Tobramycin 7 mg/kg IV EIAD **+/-** Azithromycin 500 mg IV q24h <u>Severe beta-lactam allergy (anaphylaxis, hives):</u> Vancomycin IV per pharmacy consult (initial 25mg/kg loading dose) **PLUS** Aztreonam 2 gm IV q8h **PLUS** Tobramycin 7 mg/kg IV EIAD **+/-** Levofloxacin 750mg IV q24h **+/-** Azithromycin 500 mg IV q24h **+/-** Clindamycin 600 mg IV q8h
Skin/Soft Tissue: **Necrotizing Skin/Soft Tissue: Gas Gangrene or Necrotizing Fasciitis** **(Add Clindamycin if Streptococci suspected or evidence of toxic shock syndrome present)**	Vancomycin IV - Preferred (initial loading dose of 25mg/kg) **OR** Daptomycin 6 mg/kg IV **OR** Oxacillin 2g IV Q4H **if MRSA not suspected or ruled out** Vancomycin (preferred) or Daptomycin as above **PLUS** Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours +/- Clindamycin 900mg IV Q8H