Portland VA Antibiotic Stewardship TIMEOUT

Guidelines for empiric inpatient antibiotic therapy of common conditions*

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INFECTIOUS SYNDROME		DURATION OF THERAPY
PNEUMONIA	**Assess Antibiotic Choice & Step-down Therapy with a TIMEOUT at 72 hours**	
Community-acquired (CAP)		5 days
Hospital-acquired (HAP)		7 days
Ventilator-associated (VAP)		7 days
URINARY TRACT INFECTION (UTI)		
Uncomplicated		3-5 days
Pyelonephritis		7 days
Complicated		7 days
Catheter-associated (CAUTI)		7 days
SKIN-SOFT TISSUE INFECTION (SSTI)		5-7 days
INTRA-ABDOMINAL INFECTION *[uncomplicated]*		4 days *(from date of source control)*
BLOODSTREAM INFECTION *[uncomplicated]*		
Gram-negative[+]		7 days
Staphylococcus aureus[++]		14 days
Candida spp.[++]		14 days

* This guideline is meant to assist in clinical decision-making. If questions or problems arise, please contact an Infectious Diseases consultant.

[+] Excluding *Pseudomonas aeruginosa*.

[++]Infectious Diseases consultation required.

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PNEUMONIA

Community-acquired pneumonia (CAP)- Pneumonia occurring outside of the hospital OR within <72 hours of hospital admission:

Total duration of treatment (inpatient plus post-discharge): **5 days** (unless delayed response to therapy)

Recommended *empiric* therapy:

Ceftriaxone PLUS doxycycline OR azithromycin

TIMEOUT *Re-evaluate* → at 48 hours: Check culture results/susceptibilities, fever & WBC trends, clinical status
→ at **72 hours**: Assess antibiotic choice and step-down therapy

Step-down oral therapy in patients with an appropriate clinical response:

Culture-negative cases:

Cefdinir PLUS doxycycline OR azithromycin

Culture-positive cases:

Manage according to culture results and susceptibilities

Hospital-acquired pneumonia (HAP)- Pneumonia occurring >72 hours after admission:

OR

Ventilator-associated pneumonia (VAP)- Pneumonia occurring > 72 hours after endotracheal intubation or in a chronically intubated and ventilated patient:

Total duration of treatment: **7 days** (unless delayed response to therapy)

Recommended *empiric* therapy:

Non-ICU: Ceftriaxone*

ICU: Piperacillin-tazobactam OR Cefepime*

May consider empiric vancomycin coverage for HAP/VAP until MRSA screening swab is negative.
Use of doxycycline or azithromycin is not routinely recommended.

TIMEOUT *Re-evaluate* → at 48 hours: Check culture results/susceptibilities, fever & WBC trends, clinical status

→ at **72 hours**: Assess antibiotic choice and step-down therapy

Step-down oral therapy in patients with an appropriate clinical response:

Manage according to culture results and susceptibilities

URINARY TRACT INFECTION (UTI)

Recommend empiric therapy after:

1. **Determining if the patient has symptoms**;
2. If *symptomatic*, place the order: UA/Microscopy with Cx reflex.

Uncomplicated UTI

Total duration of treatment: 3-5 days

Recommended *empiric* therapy:

Mild-moderate disease (cystitis):

1. Nitrofurantoin for 5 days OR
2. Cephalexin for 3-7 days OR
3. TMP/SMX for 3 days

Pyelonephritis

Total duration of treatment: 7 days

Recommended *empiric* therapy:

Ceftriaxone

TIMEOUT *Re-evaluate* → at 48 hours: Check culture results/susceptibilities, fever & WBC trends, clinical status

→ at **72 hours**: Assess antibiotic choice and step-down therapy

Step-down oral therapy in patients with an appropriate clinical response:

Manage according to urine culture results and susceptibilities

Complicated UTI (includes catheter-associated UTI)

Total duration of treatment: **7 days** (unless delayed response to therapy)

Recommended *empiric* therapy:

Mild-moderate disease (cystitis): Ceftriaxone

Severe disease: Piperacillin-tazobactam OR Cefepime

TIMEOUT *Re-evaluate* → at 48 hours: Check culture results/susceptibilities, fever & WBC trends, clinical status

→ at **72 hours**: Assess antibiotic choice and step-down therapy

Step-down oral therapy in patients with an appropriate clinical response:

Manage according to urine culture results and susceptibilities

Preferred agents (if active): Cephalexin, TMP/SMX or nitrofurantoin (cystitis only)

SKIN-SOFT TISSUE INFECTION (SSTI)

Non-purulent cellulitis

Total duration of treatment (inpatient plus post-discharge): **5–7 days**

Recommended *empiric* therapy:

Oral cephalexin OR IV cefazolin

TIMEOUT *Re-evaluate* → at 48 hours: Check fever & WBC trends, clinical status

→ at **72 hours**: Assess antibiotic choice and step-down therapy

Step-down oral therapy in patients with an appropriate clinical response:

Cephalexin

Purulent cellulitis with OR without abscess formation

Recommend empiric therapy after:

1. Incision and drainage of the wound for source control;
2. Submitting an aspirate or deep wound sample for gram stain and culture.

Total duration of treatment (inpatient plus post-discharge): **5–7 days**

Recommended *empiric* therapy:

IV Vancomycin OR Oral doxycycline

Promptly substitute cefazolin for vancomycin OR cephalexin for doxycycline if MRSA not identified in appropriate cultures

TIMEOUT *Re-evaluate* → at 48 hours: Check culture results/susceptibilities, fever & WBC trends, clinical status

→ at **72 hours**: Assess antibiotic choice and step-down therapy

Step-down oral therapy in patients with an appropriate clinical response:

Culture-negative cases: Recommended therapy: Cephalexin
For patients with a history of MRSA: Doxycycline

Culture-positive cases: Manage according to culture results and susceptibilities
NOTE: Recovery of resistant organism from a superficial culture does not justify broadening antimicrobial coverage in patients who have responded to narrow-spectrum therapy.

Necrotizing fasciitis

Recommend empiric therapy after:

1. Emergent surgical consultation for inspection and debridement.
2. Submitting a deep wound sample for gram stain and culture.

Total duration of treatment (inpatient plus post-discharge):

Therapy can be discontinued within 3 days after completing debridement in patients who are clinically stable

Recommended *empiric* therapy:

Piperacillin-tazobactam and vancomycin;
add clindamycin to decrease toxin production

Promptly de-escalate vancomycin if MRSA not identified in appropriate cultures

TIMEOUT *Re-evaluate* → at 48 hours: Check culture results/susceptibilities, fever & WBC trends, clinical status

→ at **72 hours**: Assess antibiotic choice and step-down therapy

Step-down oral therapy in patients with an appropriate clinical response:

Culture-negative cases: Recommended therapy: Amoxicillin/clavulanate
Patients with a history of MRSA: Amoxicillin/clavulanate plus doxycycline

Culture-positive cases: Manage according to culture results and susceptibilities
With optimized source control, recovery of a resistant organism may not require broadening antimicrobial coverage in patients who have responded to more narrow-spectrum therapy.

INTRA-ABDOMINAL INFECTION

Recommend empiric therapy after:

1. Assessing clinical severity of patient's illness (e.g. not in septic shock);
2. Evaluating abdominal pathology with appropriate imaging;
3. Consulting surgery;
4. If present, drainage of the abdominal fluid collection(s) for gram stain, cultures, and to optimize source control.

Total duration of treatment (inpatient plus post-discharge):

Therapy can be discontinued within 4 days after optimizing drainage of abdominal collection(s).
Please consider ID consultation for these cases, particularly if drainage is not complete.

Recommended *empiric* therapy:

For biliary OR enteric bacteria causing disease: Ceftriaxone plus metronidazole
(gram-negative aerobic and facultative anaerobic bacillary bacteria;
enteric gram-positive streptococci; obligate anaerobic bacillary bacteria)

For biliary or enteric bacteria causing disease after a surgical intervention: Piperacillin-tazobactam and vancomycin
OR
Cefepime, metronidazole, and vancomycin

Recommended *directed* therapy:

For biliary OR enteric bacteria causing disease:

in a patient with a history of OR risk factors for MRSA: ADD vancomycin

in a patient with a history of OR risk factors for *Enterococcus spp.*: Ceftriaxone, metronidazole, and vancomycin

in a patient with a history of OR risk factors for a multidrug-resistant organism: *Please consider ID consultation.*
(e.g. vancomycin-resistant *Enterococcus spp. (VRE),* extended-spectrum β-lactamase producing gram-negative organism (ESBL), carbapenem-resistant *Enterobacteriaceae* (CRE))

For a patient with gut perforation OR a history of/risk factors for *Pseudomonas aeruginosa*:
Piperacillin-tazobactam
OR
Cefepime plus metronidazole

TIMEOUT *Re-evaluate* → at 48 hours: Check culture results/susceptibilities, fever & WBC trends, clinical status
→ at **72 hours**: Assess antibiotic choice and step-down therapy

Step-down oral therapy in patients with an appropriate clinical response:

Manage according to culture results and susceptibilities

BLOODSTREAM INFECTION

Recommend empiric therapy after:

Drawing two sets of blood cultures (aerobic and anerobic bottles) from two different sites.
Avoid drawing blood cultures off existing catheters due to higher contamination rates.

Total duration of treatment (inpatient plus post-discharge):

Determined by organism and identifying any complicating factors such as endovascular seeding, endocarditis, device-associated infection, abscess or other nidus of infection.

For uncomplicated infection, suggestions are:

- *E. coli* OR *Klebsiella spp.*: 7 days
- *Streptococcus spp.*: 7 days
- *Staphylococcus aureus* (*ID consultation*): At least 14 days
- *Pseudomonas aeruginosa* (*ID consultation*): At least 14 days
- *Candida spp. (ID consultation)*: At least 14 days

Recommended *directed* therapy:

For uncomplicated gram-negative bacteremia,

In a patient with a history of OR risk factors for *E. coli* or *Klebsiella spp.*: Ceftriaxone

in a patient with a history of OR risk factors for ESBL gram-negative organism: *Please consider ID consultation*

in a patient with a history of OR risk factors for CRE gram-negative organism: *Please consider ID consultation*

in a patient with a history of OR risk factors for *Pseudomonas aeruginosa*: *Please consider ID consultation*

For MSSA bacteremia: Cefazolin OR Nafcillin + *ID consultation*

For MRSA bacteremia: Vancomycin + *ID consultation*

For Candidemia: Micafungin + *ID consultation*

TIMEOUT *Re-evaluate* → at 48 hours: Check culture results/susceptibilities, fever & WBC trends, clinical status

→ at **72 hours**: Assess antibiotic choice and step-down therapy

Step-down oral therapy in patients with an appropriate clinical response:

Determined after documenting microbiological clearance of bloodstream infection and culture results.

SEPSIS

Use this guidance only for patients for whom there is no apparent primary site of infection. Patients in whom sepsis is due to a specific site of infection (e.g., pneumonia, UTI) should receive antibiotics specified for that syndrome.

Total duration of treatment (inpatient plus post-discharge):

Determined by the site of infection which is identified, culture results, and optimization of source control.

- Use culture results to narrow therapy promptly, if possible.
- Reassess whether infection is the cause of illness if:
  - Cultures are negative;
  - No primary site of infection is identified.

Recommended *empiric* therapy:

For polymicrobial OR unknown cause for sepsis:

Piperacillin-tazobactam

Patients with a history of MRSA: Vancomycin PLUS piperacillin-tazobactam

OR

cefepime and metronidazole

TIMEOUT *Re-evaluate* → at 48 hours: Check culture results/susceptibilities, fever & WBC trends, clinical status

→ at **72 hours**: Assess antibiotic choice and step-down therapy

Step-down oral therapy in patients with an appropriate clinical response:

Determined by the site of infection which is identified and culture results.

APPENDIX

PNEUMONIA NOTES:

- Levofloxacin or ciprofloxacin are appropriate only if there are no other suitable oral choices.
- Other risk factors that support initiation of anti-pseudomonal therapy:
  - Severe structural lung disease (bronchiectasis), ALS, Cystic fibrosis
  - COPD with repeated exacerbations leading to frequent steroid and/or antibiotic use
  - Febrile neutropenia
- Recovery of *Pseudomonas* or another gram-negative rod from a sputum culture does not justify broadening antimicrobial coverage in patients who have responded to narrow-spectrum therapy.
- In patients with severe pneumonia or empiric treatment of MRSA or *Pseudomonas aeruginosa* pneumonia, consider drawing blood cultures.
- Penicillin-allergic patients:
  - Severe hypersensitivity (e.g., anaphylaxis, hives, Steven Johnson Syndrome): levofloxacin
  - Rash or non-specific reactions to penicillins only: cephalosporins are appropriate
- Consider viral causes for pneumonia, especially during influenza season.

UTI NOTES:

- Uncomplicated UTI:
  - Otherwise healthy individual without significant risk factors for complications
  - Signs/symptoms: dysuria, urinary frequency, urinary urgency, urinary incontinence, suprapubic tenderness
- Recurrent uncomplicated UTI:
  - 2 or more episodes of uncomplicated UTIs during the previous 6 months OR
  - 3 or more episodes during the previous 12 months
- Pyelonephritis:
  - Presence of medical condition that increases risk for pyelonephritis
  - Presence of functional or anatomical urinary tract abnormality that increases risk for pyelonephritis
  - Signs/symptoms: fever, chills, nausea, vomiting, flank pain, dysuria, urinary frequency
  - Exam findings: abdominal pain, pelvic pain or costovertebral angle tenderness
- Complicated UTI:
  - Male patients
  - Presence of indwelling catheter, stent or splint
  - Use of intermittent bladder catherization
  - Urinary post-void residual of >100 mL
  - Obstructive uropathies, such as neurogenic bladder, bladder outlet obstruction, stones and tumors
  - Vesicoureteral reflux or other genitourinary functional abnormalities
  - Urinary tract modifications, such as ileal loop or pouch
  - Chemical or radiation injuries of the uroepithelium
  - Peri- and post-operative UTI
  - Renal insufficiency, diabetes, transplantation and other relative immunosuppressive conditions
  - Signs/symptoms: fever, dysuria, urinary frequency, urinary urgency, urinary incontinence, flank or suprapubic tenderness
- Urine cultures from the prior month and the local institutional antibiogram may guide initial empiric therapy.
- Asymptomatic bacteriuria should be treated only in the context of pregnancy or prior to a urologic procedure where mucosal bleeding is anticipated (not routine placement of an indwelling catheter).
- Recovery of resistant organism from the urine does not justify broadening antimicrobial therapy in patients who have responded to narrow-spectrum therapy.
- If UTI is associated with gram-negative bacteremia, antibiotic duration is 7 days.
- Penicillin-allergic patients:
  - Severe disease/hypersensitivity (e.g., anaphylaxis, hives, Steven Johnson Syndrome): aztreonam (*Pseudomonas*)
  - Mild-moderate disease: TMP/SMX, fosfomycin or nitrofurantoin (cystitis only)
  - Rash or non-specific reactions to penicillins only: cephalosporins are appropriate
- Ciprofloxacin is appropriate only if there are no other suitable oral choices.

SSTI NOTES:

- There are high rates of resistance to clindamycin for Staphylococcus aureus in our institution.
- Recovery of resistant organism from a superficial culture does not justify broadening antimicrobial coverage in patients who have responded to narrow-spectrum therapy.
- Penicillin-allergic patients:
    - Severe hypersensitivity (e.g., anaphylaxis, hives, Steven Johnson Syndrome): aztreonam, clindamycin and vancomycin
    - Rash or non-specific reactions to penicillins only: cephalosporins are appropriate
- Doxycycline is appropriate only if there are no other suitable oral choices.
- Worsening lesion size may occur in the first 24 hours and overall improvement in both physical and laboratory markers of infection may take 48-72 hours. Early changes from guideline-based empiric therapy are not recommended in the absence of clinical instability (Clin Infect Dis 2016; 63: 1034; Clin Infect Dis 2017; 64: 214).
- Resolution of redness and swelling may take beyond seven days but is not an indication for extending antibiotic duration in the absence of other signs of infection (Scand J Infect Dis 1997; 29: 377; Cutis 2005; 75:177; Clin Infect Dis 2016; 63: 1034).
- Additional consideration should be given to the use of anti-MRSA and/or broad-spectrum gram-negative therapy in the presence of severe immunosuppression, deep puncture wound, especially while wearing shoes/sneakers, chronic wound infections, infections involving deeper structures, surgical site infections, perineal infections, periorbital infections, bite- or water-related infections. Both human bite-related infections and perineal infections warrant addition of anti-anaerobic therapy.

INTRA-ABDOMINAL INFECTION NOTES:

- Penicillin-allergic patients:
    - Severe hypersensitivity (e.g., anaphylaxis, hives, Steven Johnson Syndrome): levofloxacin
    - Rash or non-specific reactions to penicillins only: cephalosporins are appropriate
- *Enterococcus spp.* appear to be resistant to cephalosporins or fluoroquinolones.

BLOODSTREAM INFECTION NOTES:

- ID consultation is required for bacteremia due to *Staphylococcus aureus*, *Pseudomonas aeruginosa* & candidemia.
- Obtain repeat blood cultures within 24 hours of starting antibiotics to document clearance of infection.
- If subsequent repeat blood cultures remain positive, consider more serious causes for bloodstream infection, such as endovascular seeding, endocarditis, device-associated infection or other nidus of infection.
- In patients with suspected bacteremia or fungemia associated with a central venous catheter, prior to starting antimicrobial therapy:
    - Draw two sets of blood cultures (in aerobic and anaerobic bottles) from *different* peripheral sites
    - Draw one set of blood cultures from the central line
    - Remove all central venous catheters as soon as is feasible in cases of bacteremia associated with MSSA, MRSA, *Pseudomonas aeruginosa*, and candidemia
    - Draw two sets of blood cultures from different peripheral sites after line removal to document clearance of infection
- Penicillin-allergic patients with gram-negative bacteremia:
    - Severe hypersensitivity (e.g., anaphylaxis, hives, Steven Johnson Syndrome): levofloxacin
    - Rash or non-specific reactions to penicillins only: cephalosporins are appropriate

SEPSIS NOTES:

- Penicillin-allergic patients:
    - Severe hypersensitivity (e.g., anaphylaxis, hives, Steven Johnson Syndrome): levofloxacin
    - Rash or non-specific reactions to penicillins only: cephalosporins are appropriate
- Procalcitonin may be seen as an indicator of severe infection and referenced adjunct in decision-making for antibiotic selection and duration; however, more multicenter studies are needed to support routine clinical and diagnostic use.

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