Developing Hospital-specific Guidelines for the Use of Antibiotics in Adult Patients

AMR&S WORKING GROUP

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Introduction

Inappropriate inpatient use of antibiotics, including unnecessary use of broad-spectrum agents and failure to de-escalate therapy, is common in Asian hospitals.[1-9] Antibiotic treatment is also often unnecessarily prolonged and conversion from intravenous (IV) to oral therapy may not routinely occur.[10-14]

To improve antibiotic use and patient outcomes, the **Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America (IDSA/SHEA)** recommend that facility-specific clinical practice guidelines for common infectious disease syndromes should be developed as part of antimicrobial stewardship (AMS) programs.[15] Such guidelines can be adapted from pre-existing guidelines to suit resistance patterns seen at the local hospital or in the region of the hospital.[16-18] **The IDSA guidelines** can be used as a starting point when developing facility-specific guidelines.[8]

The current document provides example guidelines and templates that may be useful for hospitals developing their own facility-specific guidelines. It is essential that each hospital accounts for local patterns of resistance and antibiotic availability. The example guidelines and templates are intended to assist in the rational empiric selection of antibiotics based on the most likely causative organism for infections commonly treated in Asian hospitals. In addition to antibiotic recommendations, the example guidelines and templates contain information regarding appropriate de-escalation of broad-spectrum agents and/or conversion from IV to oral antibiotics.

It is important to note that guidelines are not intended to replace clinical judgment in individual cases. Expert infectious disease consultation is recommended for all complex infections or immunocompromised patients.

To develop hospital-specific guidelines for your hospital, we recommend following the steps below:

Step 1 – Identify the most important infectious disease syndrome(s) in your hospital requiring treatment guidelines

Step 2 – Integrate the care bundle guidance of the specific clinical syndrome(s), including the necessary clinical or laboratory tasks for diagnosis or differential diagnosis

Step 3 – Evaluate the most common pathogens of the specific clinical syndrome(s) in your hospital with reference to the **antibiogram**

Step 4 – Evaluate effective antimicrobial agents that are available for the treatment of the specific clinical syndrome(s) and prioritize them. Review the latest international guidelines (eg, IDSA guidelines) on the relevant syndrome(s) and adapt these recommendations based on your local epidemiology, where applicable. If specific recommendations have not been made for certain resistant organisms, a detailed literature search should be conducted before any proposed choices are made, to make sure that the choices are based on strong evidence (eg, trials, case reports, systematic reviews and meta-analyses on the effectiveness of specific antibiotic combinations against resistant organisms)[19]

Step 5 – Integrate all the above information into a table or an algorithm. Include footnotes as needed to highlight important endemic diseases relevant within the specific syndrome(s) in the country or area (eg, melioidosis in community-acquired pneumonia in Southeast Asia)

Step 6 – Emphasize the importance of considering patient factors (eg, kidney and hepatic function, antibiotic history, immunocompromised status), the metabolism pathway of the antibiotics to be prescribed and potential drug-drug interactions before deciding on a suitable treatment plan and dosage[20]

Index of example guidelines and templates for the use of antibiotics in adult patients

General principles of antibiotic use in hospitalized patients

Answering the following key questions will help you to select the most appropriate antibiotic for the initial treatment of your patient.

1. **What is the diagnosis/most likely cause of infection?** Antibiotics should not be prescribed without clear suspicion or evidence of infection.[20]

2. **How severe is the infection?** Early broad-spectrum therapy should be reserved for patients with severe infections.[20,21]

3. **What is the risk of infection with drug-resistant organisms?** It is important to assess risk factors for drug-resistant pathogens.[14,20] Consider recent hospitalizations and resistance patterns of all units to which the patient has been admitted, as well as the patient's recent antibiotic history, because patients who have been hospitalized recently, undergone invasive procedures and/or been treated with antibiotics are at increased risk of infection with drug-resistant bacteria.[14,20]

4. **Is the patient immunocompromised?** Hospitalized patients who are immunocompromised are at increased risk of life-threatening multidrug-resistant infections and often require broad-spectrum antibiotics.[14,22]

5. **Does the patient have an antibiotic allergy?** It is important to distinguish non-allergic adverse reactions from true allergic reactions. Some patients report that they are allergic to penicillin when they have had a non-allergic adverse reaction, and this may result in unnecessary avoidance of the most effective narrow-spectrum antibiotic.[20]

6. **What is the status of the patient's kidney and hepatic function? Is the patient taking any other medications?** Antibiotic doses must be adjusted properly to minimize side effects and drug interactions. In patients with impaired kidney or liver function, or in those taking enzyme inhibitors, dose reduction might be required to prevent drug accumulation and toxicity. However, sometimes doses might need to be increased to avoid underdosing young healthy patients with rapid renal elimination or those with rapid hepatic metabolism due to concomitant use of enzyme inducers such as rifampicin or phenytoin.[14,20]

Care bundles (small sets of measurable, evidence-based practices) can be used to ensure that the appropriate questions are answered and to support the implementation of antibiotic prescribing guidelines.[23,24] Care bundle practices should be consistently performed by prescribers before and during antibiotic treatment.[24]

Example of a treatment care bundle[24]

At the start of treatment:
- Provide a clinical rationale for antibiotic treatment
- Send the appropriate specimens to the microbiology laboratory
- Select antibiotic therapy according to hospital guidelines and the patient's risk profile, including risk of infection with drug-resistant organisms, immunologic status and any antibiotic allergy
- Consider removal of any foreign body, drainage of pus or other surgical intervention, as appropriate

During treatment:
- Daily consideration of the feasibility of modification, de-escalation, escalation, IV-to-oral-conversion or discontinuation of antibiotic treatment based on the clinical picture and laboratory results
- Monitoring of antibiotic drug levels, as feasible and as needed

Empiric use of carbapenems

When compiling guidelines, thought should be given to **WHO priority antibiotic-resistant pathogens**.[25] The three pathogens deemed a critical priority (carbapenem-resistant *Acinetobacter baumannii*, carbapenem-resistant *Pseudomonas aeruginosa* and carbapenem-resistant, ESBL-producing Enterobacteriaceae) can cause severe and often deadly infections in hospitalized patients.[25] However, inappropriate use of carbapenems, which are often empirically prescribed for the treatment of healthcare-associated and hospital-acquired infections in Asian settings where ESBL-producing Enterobacteriaceae are endemic, is helping to drive resistance.[2,8,9,26,27] An example of guidelines for the appropriate empiric use of carbapenems is provided in Table 1.

De-escalation

Appropriate specimens should be collected and sent for Gram stain and culture before starting antibiotic therapy.[14,20] Once microbiology results are available, empiric therapy should be changed to the most active antibiotic(s) with the narrowest possible spectrum based on culture and susceptibility results.[14,20] In the meantime, if the hospital's empiric antibiotic treatment guidelines have not been followed without a valid reason, broad-spectrum empiric therapy can be de-escalated in clinically stable patients (Box 1) in accordance with hospital guidelines.[9,28]

Box 1. Criteria for de-escalation of broad-spectrum empiric therapy[9]

Temperature <38°C for 24h
Systolic blood pressure returned to baseline or ≥100 mmHg
Not on inotropes
Respiratory rate <25 breaths per minute
Not mechanically ventilated
Oxygen saturation ≥92% on room air

IV-to-oral conversion

Certain patients should be switched from IV to oral antibiotics as soon as they are hemodynamically stable, improving clinically and able to tolerate oral medication (Figure 1).[14,20] Fluoroquinolones and macrolides are examples of antibiotics with excellent oral bioavailability that are suitable for automatic IV-to-oral conversion of the same drug.[29,30] Depending on the clinical situation and/or microbiology results, IV antibiotics without equivalent oral formulations can also be switched to oral agents that have similar activity or de-escalated to narrower-spectrum oral agents.[31]

Table 1

Example guidelines* for the empiric use of carbapenems (as used at Singapore General Hospital)[29]

*EXAMPLE ONLY – MUST BE ADAPTED TO LOCAL RESISTANCE PATTERNS AND ANTIBIOTIC AVAILABILITY

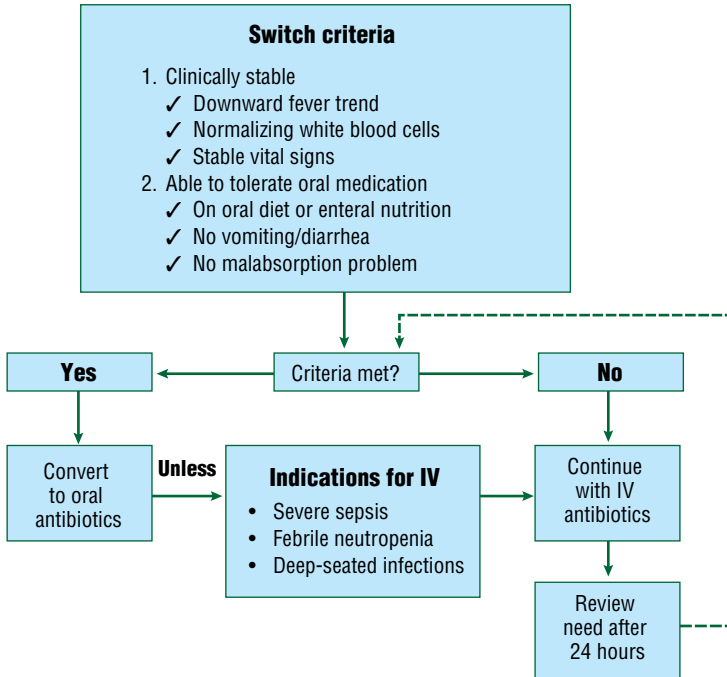| |
|---|
| **Criteria A (must fulfill all 3)**
1. Sepsis
AND
2. Clinically unwell (drowsy/confused, oxygen saturation <92%, SBP <90 mmHg OR respiratory rate >30 breaths/minute)
AND
3. Hospital-acquired (48 hours after admission) or healthcare-associated[a] infection |
| **Criteria B (must fulfill both)**
1. Patients with severe hospital-acquired and healthcare-associated infections who fail to improve after 48–72 hours of empiric therapy as per hospital empiric antibiotic treatment guidelines
AND
2. Appropriate cultures remain negative |
| **Criteria C**
Prescribed according to hospital empiric antibiotic treatment guidelines |
| **Criteria D**
Empiric therapy for hospital-acquired organ infection when a delay in appropriate therapy could pose catastrophic risk |

SBP, systolic blood pressure

[a]Healthcare-associated infections can be defined when there is ≥1 of the following risk factors: hospitalization in an acute care hospital for ≥2 days in the last 90 days, residence in a nursing home or long-term care facility in the last 90 days, receiving outpatient IV therapy within the past 30 days, dialysis within the last 30 days.

Figure 1

Example guidelines* for IV-to-oral conversion of antibiotics (as used at Singapore General Hospital)[8,29]

*EXAMPLE ONLY – MUST BE ADAPTED TO LOCAL RESISTANCE PATTERNS AND ANTIBIOTIC AVAILABILITY

Switch criteria

1. Clinically stable
   - ✓ Downward fever trend
   - ✓ Normalizing white blood cells
   - ✓ Stable vital signs
2. Able to tolerate oral medication
   - ✓ On oral diet or enteral nutrition
   - ✓ No vomiting/diarrhea
   - ✓ No malabsorption problem

| Yes | ← | Criteria met? | → | No |

Convert to oral antibiotics **Unless** → **Indications for IV**
- Severe sepsis
- Febrile neutropenia
- Deep-seated infections

→ **Continue with IV antibiotics**

Review need after 24 hours

Adapted from Teo J, et al. 2012; and Singapore General Hospital Antimicrobial Guidelines 2014.

Empiric antibiotic treatment guidelines

Example guidelines are provided for the empiric treatment of sepsis (Table 2) and urinary tract infections (Table 3). The recommendations for empiric antibiotic selection made in these examples are based on those of international guidelines.[32,33] Rather than recommending specific antibiotics, the examples in the tables make general antibiotic drug class recommendations that are intended to assist in the rational empiric selection of antibiotics based on the most likely causative organism for infections commonly treated in Asian hospitals. These recommendations may not be appropriate for all settings. After careful consideration of local epidemiology data and susceptibility patterns seen on hospital or local **antibiograms**, general druvg class recommendations can be replaced with recommendations for specific antibiotics from the hospital formulary.

Appendices 1–4 contain syndrome-specific example templates for empiric therapy – these have to be filled and adapted based on hospital or local settings. Syndromes include hospitalized community-acquired pneumonia (CAP) (Appendix 1), and hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) (Appendix 2). Appendix 3 provides an example template for patients with skin and soft tissue infections (including cellulitis, necrotizing fasciitis and surgical site infections) and Appendix 4 is an example template for intra-abdominal infections. Links to full online versions of the relevant international guidelines are provided within each table. However, when local guidelines are available, Asian hospitals should use these as a starting point when developing hospital-specific antibiotic treatment guidelines.

Some of the tables contain example guidance regarding appropriate switch from IV to oral antibiotics during therapy. However, as part of the care bundle approach, hospital antibiotic guidelines should provide detailed guidance in relation to changing empiric treatment to definitive pathogen-directed therapy once laboratory culture and susceptibility results are known. Such detailed guidance is beyond the scope of the examples in the tables provided here.

Example guidelines* for the empiric treatment of adults with sepsis or septic shock[32]

***EXAMPLE ONLY – MUST BE ADAPTED TO
LOCAL RESISTANCE PATTERNS AND ANTIBIOTIC AVAILABILITY**

Sepsis or septic shock	
Initial empiric treatment[a,b,c,d]	**Duration of therapy**

• For patients at high risk of MRSA, use antibiotics with MRSA coverage
• For patients at low risk of MRSA, use antibiotics without MRSA coverage
• For patients at high risk of MDR organisms, use two antibiotics with Gram-negative coverage[e]
• For patients at low risk of MDR organisms, use one Gram-negative agent
	• Assess daily for de-escalation rather than having a fixed duration of therapy
	• If there is adequate source control:
	  · Use shorter rather than longer duration
	  · If optimal duration is unclear, use procalcitonin AND clinical evaluation to decide when to discontinue therapy

[a]In patients with possible septic shock or a high likelihood for sepsis, administer antimicrobials immediately, ideally within 1 hr of recognition

[b]In patients with possible sepsis without shock, rapidly assess the likelihood of infectious vs noninfectious causes of acute illness; if concern for infection persists, administer antimicrobials within 3 hrs of first recognition of sepsis

[c]In patients with suspected sepsis or septic shock but unconfirmed infection, continuously re-evaluate and search for alternative diagnoses and discontinue empiric antimicrobials if an alternative cause of illness is demonstrated or strongly suspected

[d]For maintenance (after an initial bolus) using beta-lactams, use prolonged infusion rather than conventional bolus infusion

[e]Do not use double Gram-negative coverage once the causative pathogen and susceptibilities are known

• **Refer to local guidelines if available. Online link to the SCCM/ESICM Surviving Sepsis Campaign 2021 Adult Guidelines: https://www.sccm.org/clinical-resources/guidelines/guidelines/surviving-sepsis-guidelines-2021**

ESICM, European Society of Intensive Care Medicine; MDR, multiple-drug resistant; MRSA, methicillin-resistant *Staphylococcus aureus*; SCCM, Society of Critical Care Medicine

Table 3

Example guidelines* for the empiric treatment of catheter-associated urinary tract infections[33]

Catheter-associated urinary tract infection (CA-UTI)[a]	
Initial IV or oral empiric treatment[b,c,d]	**Total duration of therapy**
• Trimethoprim-sulfamethoxazole or • Fluoroquinolone	• 7 days if prompt resolution of symptoms • 10–14 days if delayed response • 3 days if catheter removed in female patient ≤65 years with lower tract infection
[a]Routine screening and treatment of patients with catheter-associated asymptomatic bacteriuria is not recommended [b]CA-UTIs are often polymicrobial and caused by MDR uropathogens. Urine cultures are recommended before starting antimicrobial therapy [c]Remove catheters (whenever possible) and obtain urine culture from a voided midstream urine, or replace long-term catheters and obtain urine culture from the freshly placed catheter before starting antibiotics [d]Regimens should be adjusted as appropriate based on culture, susceptibility results and the clinical course	
• **Refer to local guidelines if available. Online link to the IDSA CA-UTI treatment guideline: www.idsociety.org/practice-guideline/alphabetical-guidelines/**	

Potentially useful resources

This is a list of some institutions that have provided online access to their antibiotic guidelines:

- Johns Hopkins Medicine (**https://www.hopkinsmedicine.org/antimicrobial-stewardship/guidelines/**)
- Sinai Health System + University Health Network (**www.antimicrobialstewardship.com/treatment**)
- Stanford Antimicrobial Safety and Sustainability Program (**med.stanford.edu/bugsanddrugs/guidebook.html**)
- UCLA Health (**asp.mednet.ucla.edu/pages/guidebook**)
- Wake Forest School of Medicine (**https://school.wakehealth.edu/departments/internal-medicine/infectious-diseases/cause/antimicrobial-disease-treatment-and-dosing-guidelines**)

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Appendices

Appendix 1

Example template* for the empiric treatment of patients hospitalized with community-acquired pneumonia

Hospitalized community-acquired pneumonia (CAP)			
Choice for initial empiric treatment		Choice for switching from IV to oral treatment[e]	Total duration[f]
Non-severe CAP[a,b,c]	Severe CAP[b,c,d]		
[To be filled based on local patterns of resistance and antibiotic availability]	[To be filled based on local patterns of resistance and antibiotic availability]	[To be filled based on local patterns of resistance and antibiotic availability]	[To be filled based on local patterns of resistance and antibiotic availability]

[a] Obtain pretreatment Gram stain and culture of lower respiratory secretions, as well as blood cultures in patients who are being empirically treated for MRSA or *P. aeruginosa*; were previously infected with MRSA or *P. aeruginosa*; or were hospitalized and received parenteral antibiotics in the last 90 days.

[b] Initiate empiric antibiotic therapy in patients with clinically suspected and radiographically confirmed CAP regardless of initial serum procalcitonin level

[c] Cover for MRSA or *P. aeruginosa* only if locally validated risk factors for either pathogen are present; if treating on the basis of published risk factors without local etiological data, continue empiric coverage while obtaining culture data to establish if these pathogens are present

[d] Obtain pretreatment Gram stain and culture of lower respiratory secretions, as well as blood cultures

[e] Use either the same agent or the same drug class

[f] Use a validated measure of clinical stability (resolution of vital sign abnormalities [heart rate, respiratory rate, blood pressure, oxygen saturation, and temperature], ability to eat, and normal mentation) to guide duration of therapy, continuing antibiotic therapy until the patient achieves stability for ≥5 days or 7 days for MRSA or *P. aeruginosa*

*This is a template only. The table must be filled and adapted based on local/hospital patterns of resistance and antibiotic availability. Recommendations in the footnote are based on the IDSA/ATS treatment guidelines and should be adapted as appropriate

- **Refer to local guidelines if available. Online link to the IDSA/ATS CAP treatment guidelines: www.idsociety.org/practice-guideline/community-acquired-pneumonia-cap-in-adults/**

ATS, American Thoracic Society; ICU, intensive care unit; IDSA, Infectious Diseases Society of America; IV, intravenous; MRSA, methicillin-resistant *Staphylococcus aureus; P. aeruginosa, Pseudomonas aeruginosa*

Reference: Metlay JP, 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. *Am J Respir Crit Care Med* 2019;200:e45-e67.

Appendix 2

Example template* for the empiric treatment of hospital-acquired pneumonia and ventilator-associated pneumonia

Hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP)				
Choice for initial empiric treatment			Choice for oral treatment (conversion or de-escalation)	Total duration
HAP[a]		VAP[b,c]		
No ventilatory support	Ventilatory support			
[To be filled based on local patterns of resistance and antibiotic availability]	*[To be filled based on local patterns of resistance and antibiotic availability]*	*[To be filled based on local patterns of resistance and antibiotic availability]*	*[To be filled based on local patterns of resistance and antibiotic availability]*	*[To be filled based on local patterns of resistance and antibiotic availability]*

[a] Pneumonia not incubating at the time of hospital admission and occurring ≥48 hours after admission

[b] Pneumonia occurring >48 hours after endotracheal intubation

[c] Suggest including two antipseudomonal antibiotics from different classes only when risk factors for antimicrobial resistance are present (eg, prior IV antibiotic use within 90 days, septic shock at the time of VAP, ≥5 days of hospitalization before VAP), patients in units where >10% of Gram-negative isolates are resistant to the agent being considered for monotherapy, and patients in an ICU where local antimicrobial susceptibility is not known

This is a template only. The table must be filled and adapted based on local/hospital patterns of resistance and antibiotic availability. Recommendations in the footnote are based on the IDSA/ATS treatment guidelines and should be adapted as appropriate
- **Refer to local guidelines if available. Online link to the IDSA/ATS CAP treatment guidelines:**
  https://www.idsociety.org/practice-guideline/hap_vap/

ATS, American Thoracic Society; IDSA, Infectious Diseases Society of America; IV, intravenous
Reference: Kalil AC, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *Clin Infect Dis* 2016;63:e61-e111.

Appendix 3

Example template* for the empiric treatment of patients hospitalized with skin and soft tissue infections

Hospitalized skin and soft tissue infections (SSTIs)							
Choice for initial empiric IV treatment					Duration of therapy and conversion to oral therapy		
Cellulitis[a,b]		Necrotizing fasciitis[c]	Surgical site infections[a,d,e]		Cellulitis	Necrotizing fasciitis	Surgical site infections
Moderate infection	Severe infection		Operations of the head, trunk, extremity	Operations of the GI tract or female genital tract			
[To be filled based on local patterns of resistance and antibiotic availability]	[To be filled based on local patterns of resistance and antibiotic availability]	[To be filled based on local patterns of resistance and antibiotic availability]	[To be filled based on local patterns of resistance and antibiotic availability]	[To be filled based on local patterns of resistance and antibiotic availability]	[To be filled based on local patterns of resistance and antibiotic availability]	[To be filled based on local patterns of resistance and antibiotic availability]	[To be filled based on local patterns of resistance and antibiotic availability]

TEMPLATE ONLY

[a] Patients with systemic signs of infection (eg, temperature >38°C, heart rate >90 beats/min, respiratory rate >24 breaths/min)

[b] Patients with mild cellulitis (no systemic signs of infection) should receive oral outpatient therapy with an antistreptococcal agent

[c] Modify antibiotic therapy once definitive microbiological results have been obtained

[d] Surgical patients with <5 cm of erythema and induration with minimal systemic signs of infection do not require antibiotics

[e] Suggest using an agent effective against MRSA when MRSA risk factors are present (eg, prior MRSA infection, recent antibiotics)

*This is a template only. The table must be filled and adapted based on local/hospital patterns of resistance and antibiotic availability. Recommendations in the footnote are based on the IDSA SSTI treatment guidelines and should be adapted as appropriate
- **Refer to local guidelines if available. Online link to the IDSA SSTI treatment guidelines: https://www.idsociety.org/practice-guideline/skin-and-soft-tissue-infections/**

GI, gastrointestinal; IDSA, Infectious Diseases Society of America; IV, intravenous; MRSA, methicillin-resistant _Staphylococcus aureus_

Reference: Stevens DL, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 Update by the Infectious Diseases Society of America. _Clin Infect Dis_ 2014;59:e10-e52.

Appendix 4

Example template* for the empiric treatment of intra-abdominal infections

Intra-abdominal infections (IAIs)					
Choice for initial IV empiric treatment				**Conversion to oral therapy**	**Total duration**
Community-acquired IAI[a,b,c]		**Healthcare-associated IAI[d]**			
Single-agent therapy	**Combination regimens[c]**	**Single-agent therapy**	**Combination therapy**		
[To be filled based on local patterns of resistance and antibiotic availability]	*[To be filled based on local patterns of resistance and antibiotic availability]*	*[To be filled based on local patterns of resistance and antibiotic availability]*	*[To be filled based on local patterns of resistance and antibiotic availability]*	*[To be filled based on local patterns of resistance and antibiotic availability]*	*[To be filled based on local patterns of resistance and antibiotic availability]*

[a]For patients with mild-to-moderate community-acquired infections, regimens without substantial antipseudomonal activity are preferred

[b]Empiric use of broad-spectrum regimens against Gram-negative organisms is recommended for patients with severe community-acquired IAI. This should be tailored once culture and susceptibility reports are available

[c]In high-risk community-acquired IAI, quinolones should not be used unless hospital surveys indicate >90% susceptibility of *Escherichia coli* to quinolones

[d]Empiric therapy for healthcare-associated IAI should be driven by local microbiology. Multidrug regimens may be needed to achieve empiric coverage of likely pathogens – broad-spectrum antibiotics should be tailored upon availability of culture and susceptibility reports

*This is a template only. The table must be filled and adapted based on local/hospital patterns of resistance and antibiotic availability. Recommendations in the footnote are based on the Surgical Infection Society/ IDSA treatment guidelines and should be adapted as appropriate

- **Refer to local guidelines if available. Online link to Surgical Infection Society/IDSA guidelines:**
  https://www.idsociety.org/practice-guideline/alphabetical-guidelines/

IDSA, Infectious Diseases Society of America; IV, intravenous

Reference: Solomkin JS, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: Guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. *Clin Infect Dis* 2010;50:133-164.

Updated guidelines for IAIs are currently in development (as of August 2022)