PALLIATIVE PEARLS
BY ENCLARA PHARMACIA

Antibiotic Use: Decision-Making Guidance for Hospice Care

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Lack of clear, evidence-based guidelines for antibiotic use in patients at the end-of-life challenges decision making for the palliative clinician.[1] Antibiotic use may prevent hospitalizations but increases the risk of adverse effects and drug interactions. Use may also complicate or prevent the transition of an institutionalized patient to the home; many symptoms may be managed with other treatments, such as antipyretics or opioids, with less adverse effects and potential drug interactions.[2]"

This month's topic provides antibiotic use shared decision-making guidance, focusing on how to approach conversations with patients and caregivers, alternative symptom management, and empiric therapy recommendations for indications commonly encountered by Enclara pharmacists.

Overview

Antibiotics are currently overused in hospice and palliative care settings.[3-7] Before initiating therapy, it is important to first consider patient-specific variables and the potential challenges of antibiotic use.

Aspect	Consideration(s)
Patient Prognosis	Assessing the underlying illness and estimated life expectancy[1]
Symptom Improvement vs. Burden	Weighing the potential benefits of symptom relief against the burdens of antibiotic therapy[1]
Variability in Prescribing	Absence of standardized guidelines leads to inconsistent antibiotic use[1]
Uncertain effectiveness	Limited evidence on the ability of antibiotics to improve symptoms and quality of life in terminally ill patients
Adverse Effects	Antimicrobial-associated diarrhea (e.g., *Clostridioides difficile* infection (CDI)) risk increases 7-10 times) Seizures (particularly with beta-lactams) Diarrhea, stomach cramps[1,8]
Other Patient Burdens	Intravenous antibiotics may cause phlebitis or infections Oral antibiotics can be challenging for patients with swallowing difficulties[1] Comprehensive assessment of an infection may be invasive (e.g., blood draws, chest x-rays)
Costs Without Benefit	High expenses can impact care plans and resource allocation.[1] Antibiotic administered unnecessarily for a viral infection

Drug Interactions	Assess the medication profile for both polypharmacy and antibiotic drug interactions which include but are not limited to:[8,21] • Ciprofloxacin (Cipro®) used with tizanidine (Zanaflex®) may increase the serum concentration of tizanidine and is contraindicated • Anti-infectives ciprofloxacin, sulfamethoxazole-trimethoprim (Bactrim®), metronidazole (Flagyl®), erythromycin, and/or fluconazole (Diflucan®) used with warfarin may increase INR levels • Nitrofurantoin use in patients with creatinine clearance (CrCl) < 30ml/min may lead to toxicity • Bactrim® used with an ACE inhibitor (e.g., lisinopril (Prinivil®)) or angiotensin receptor blocker (e.g., losartan (Cozaar®)) with renal disease may lead to hyperkalemia
Antibiotic Resistance	Multiple antibiotic therapy courses may lead to development of multidrug resistant organisms (MDRs)

Foster Shared Decision-Making

Ensure that antibiotic use aligns with the patient's and family's objectives and preferences.[1,2,8] Karlin D, et al (2024)[2] outlines recommendations for clinician collaboration and patient and caregiver approaches by disease stage:

Early stages – Set expectations (achieving source control and clearing infection) and collaborate with other teams on consistent messaging.

Middle stages – Discuss trade-offs in treatment (adverse effects from antimicrobials such as gastrointestinal intolerance, volume overload, increasing resistance), decreasing likelihood of source control, and initiate conversations around goals of care.

Later stages and end of life – Explore goals of care with the REMAP framework[2,9]

R	Reframe the situation	• Clarify current understanding of the expected clinical trajectory and the rationale for revisiting goals of care. • If additional prognostic information needs to be communicated, this information should be communicated succinctly and with empathy.
E	Explore emotions	• Address the underlying emotion driving the request for antimicrobials, rather than solely providing information (e.g., address guilt ("You've done everything possible"), fear of causing harm, and overwhelmed feelings.)
M	Map out goals and values	• Explore hopes for specific outcomes, such as going home (if hospitalized) or spending time with family. • Contrast the potential lack of benefit from antimicrobials with the care at home with hospice. • Whenever possible, transition to oral regimens.
A	Align with expressed values	• Reflect what you have heard as the patient's core values and preferences to ensure that you have an accurate understanding of the priorities.

P	Plan out next steps	• Proceeding with interventions aimed at prolonging life, potentially as a time-limited trial.[10] • Continuing current level of medical support without further escalation.

Symptom Palliation

The below symptom management and antibiotic guidance relates to the most treated infections in the hospice population, urinary tract infections (UTIs) and respiratory infections. For information on skin infections, refer to the bacterial infection section of Back to Basics: Skin Conditions & Topical Treatment.

Consider Alternative Symptom Management

Utilize other medications to manage symptoms without antibiotics:[1,2,8,11,12]

Symptom(s)	Alternative Symptom Management
Fever[15-17]	• Managing fever may include cold baths, encouragement of clear liquid intake to prevent dehydration, maintaining a comfortable room temperature, and wearing of lightweight clothing • Acetaminophen, NSAIDs (e.g., ibuprofen)
Urinary: Pain, Spasms[14,15]	• Remove foley catheter, if possible, increase water intake, and the use of cranberry juice and vitamin C supplementation • Urinary Pain: Phenazopyridine (Pyridium®) • Urinary Spasms: Oxybutynin (Ditropan®)
Respiratory: Dyspnea and/or cough[15,18]	Dyspnea: • Use fans, open windows if safe, breathing exercises, head and body positioning, limit strenuous activity, minimize stress, and employ relaxation techniques • Opioids, albuterol Cough: • Use chest physiotherapy, elevate head of bed, use a humidifier, water hydration, and smoking cessation • For mild symptoms, consider benzonatate • For moderate or severe symptoms (or insufficient response to benzonatate), consider initiating morphine at a low dose or gabapentin (Neurontin®) or pregabalin (Lyrica®) therapy • For cough with thick sputum, add an expectorant (e.g., guaifenesin, nebulized saline) or mucolytic (acetylcysteine (Mucomyst®)) • For cough with bronchospasm, add a bronchodilator like inhaled albuterol • For cough and excess secretions, add an anticholinergic agent like glycopyrrolate

Initiate Antibiotics Only When Appropriate

- Implement trials of antibiotic therapy with a specific days' supply and predefined evaluation periods and criteria for continuation or cessation.[2,11]
- Prescribe oral antibiotics whenever feasible to reduce administration burdens. Use oral suspensions for patients with difficulty swallowing solid dosage forms.[2,11]
- Hospice patient goals of care commonly do not include collection of urine or sputum for purposes of culture and sensitivity testing. Empirically treat based on suspected organism.
- Many antibiotic doses require adjustment for renal impairment. Review drug information or consult an Enclara pharmacist for specific guidance.[20,21]

Empiric Therapy Recommendations for Indications Commonly Encountered by Enclara Pharmacists

In the tables below, you will find empiric therapy recommendations for the following infections:

- Uncomplicated urinary tract infection (cystitis)
- Complicated urinary tract infection (pyelonephritis)
- Catheter-associated urinary tract infection
- Community-acquired pneumonia in the outpatient setting

Management of recurrent urinary tract infections (i.e., prophylaxis) requires patient historical culture and/or sensitivity data for appropriate therapy selection.[14] Causative organisms in upper respiratory tract infections (e.g., sinusitis, pharyngitis, tonsilitis) may be bacterial (e.g., streptococcal) or viral (e.g., COVID-19, seasonal influenza, mononucleosis, rhinovirus) prompting outpatient evaluation and testing to identify the best management strategy.[17,19] These two infection types will not be covered in this resource.

Uncomplicated Urinary Tract Infection (Cystitis)[14,22,23]
Symptoms: Normal genitourinary tract with no signs of obstruction and symptoms (urinary frequency, urinary urgency, foul-smelling urine, burning with urination, hematuria, dark, cloudy urine, fever, suprapubic discomfort) are confined to the lower urinary tract.
Common organisms: *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Staphylococcus saprophyticus*

Empiric therapy:
Indication: No risk of infection with multidrug resistance (MDR) gram-negative organism:*
• Trimethoprim-sulfamethoxazole (Bactrim DS®) 160mg-800mg# by mouth twice daily for 3 days or
• Nitrofurantoin macrocrystal (Macrobid®)† 100mg by mouth twice daily for 5 days or
• Fosfomycin (Monurol®) granules 3 grams, dissolved in 3 to 4 ounces of water, as a single dose or
• Alternatives:
  ○ Beta-lactam antibiotic for 5 to 7 days (avoid ampicillin or amoxicillin monotherapy due to lower efficacy rates)
  ▪ Amoxicillin-clavulanate (Augmentin®) 500 mg-125# mg by mouth twice daily or
  ▪ Cefpodoxime (Vantin®) 100 mg# by mouth twice daily or
  ▪ Cefdinir (Omnicef®) 300 mg# by mouth twice daily or

        - Cefadroxil (Duricef®) 500mg# by mouth twice daily or
        - Cephalexin (Keflex®) 500 mg# by mouth twice daily or
    - Beta-lactam allergy or intolerance, fluoroquinolone antibiotic for 3 days (avoid moxifloxacin due to limited urinary concentrations)
        - Ciprofloxacin (Cipro®) 250 mg# by mouth twice daily or
        - Ciprofloxacin extended-release (Cipro® XR) 500 mg# by mouth daily or
        - Levofloxacin (Levaquin®) 250 mg# by mouth daily

Indication: Risk of infection with multidrug resistance (MDR) gram-negative organism:*

- Nitrofurantoin macrocrystal (Macrobid®)† 100mg by mouth twice daily for 5 days or
- Fosfomycin (Monurol®) granules 3 grams, dissolved in 3 to 4 ounces of water, as a single dose or
- Alternatives:
    - See *Complicated Urinary Tract Infection (Pyelonephritis)*

* Risk factors for multidrug resistance (MDR) gram-negative UTIs include any one of the following in the prior three months:

- An MDR, gram-negative urinary isolate, including a fluoroquinolone-resistant *Pseudomonas.*
- Inpatient hospital stays or residence in a healthcare facility (e.g., nursing facility).
- Use of a fluoroquinolone, trimethoprim-sulfamethoxazole, or broad-spectrum beta-lactam.
- Travel to parts of the world with high rates of MDR organisms (e.g., India, Israel, Spain, and Mexico).

Dose requires adjustment for renal insufficiency.[20,21]

† Avoid this medication in patients with CrCl < 30 ml/min.[20,21]

Complicated Urinary Tract Infection (Pyelonephritis)[13,22,23]

Symptoms: Upper back or flank pain, fever and chills, rigors, nausea and vomiting, pyuria, fatigue, delirium.

Common organisms: *Escherichia coli, Klebsiella* spp., *Proteus* spp., *Pseudomonas aeruginosa, Enterococcus* spp., methicillin-sensitive *Staphylococcus aureus,* methicillin-resistant *Staphylococcus aureus*

Empiric therapy:

Indication: No risk of infection with multidrug resistance (MDR) gram-negative organism:*

- For patients with low risk of fluoroquinolone resistance/toxicity:
    - Ciprofloxacin (Cipro®) 500 mg# by mouth twice daily for 5 to 7 days or
    - Ciprofloxacin extended-release (Cipro® XR) 1000 mg# by mouth daily for 5 to 7 days or
    - Levofloxacin (Levaquin®) 750 mg# by mouth daily for 5 to 7 days
- If the community prevalence of fluoroquinolone resistance in *Escherichia coli* is known to be >10%, give one dose of a long-acting parenteral agent prior to the fluoroquinolone:
    - Ceftriaxone (Rocephin®) 1 gram# intravenously or intramuscularly once or
    - Ertapenem (Invanz®) 1 gram# intravenously or intramuscularly once or
    - Gentamicin 5 mg/kg# intravenously or intramuscularly once or

  - Tobramycin 5 mg/kg# intravenously or intramuscularly once

- For patients who cannot use a fluoroquinolone, give one dose of a long-acting parenteral agent:
  - Ceftriaxone (Rocephin®) 1 gram# intravenously or intramuscularly once or
  - Ertapenem (Invanz®) 1 gram# intravenously or intramuscularly once or
  - Gentamicin 5 mg/kg# intravenously or intramuscularly once or
  - Tobramycin 5 mg/kg# intravenously or intramuscularly once

  Followed by:
  - Trimethoprim-sulfamethoxazole (Bactrim DS®)# 1 tablet by mouth twice daily for 7 to 10 days or
  - Amoxicillin-clavulanate (Augmentin®) 875 mg# by mouth twice daily for 7 to 10 days or
  - Cefpodoxime (Vantin®) 200 mg# by mouth twice daily for 7 to 10 days or
  - Cefadroxil (Duricef®) 1 gram# by mouth twice daily for 7 to 10 days

Indication: Risk of infection with multidrug resistance (MDR) gram-negative organism*

- Ertapenem (Invanz®) 1 gram# intravenously or intramuscularly once; followed by:
  - Ciprofloxacin (Cipro®) 500 mg# by mouth twice daily for 5 to 7 days or
  - Ciprofloxacin extended-release (Cipro® XR) 1000 mg# by mouth daily for 5 to 7 days or
  - Levofloxacin (Levaquin®) 750 mg# by mouth daily for 5 to 7 days

* Risk factors for multidrug resistance (MDR) gram-negative UTIs include any one of the following in the prior three months:
  - An MDR, gram-negative urinary isolate, including a fluoroquinolone-resistant *Pseudomonas.*
  - Inpatient hospital stays or residence in a healthcare facility (e.g., nursing facility).
  - Use of a fluoroquinolone, trimethoprim-sulfamethoxazole, or broad-spectrum beta-lactam.
  - Travel to parts of the world with high rates of MDR organisms (e.g., India, Israel, Spain, and Mexico).

Dose requires adjustment for renal insufficiency.[20,21]

Catheter-Associated Urinary Tract Infection[24,25]

Symptoms: Common presentation includes fever, flank pain, costovertebral angle tenderness, and/or systemic signs or symptoms of infection, like pyelonephritis, with pyuria and bacteriuria. Some patients (e.g., those who have recently had a urethral catheter removed) present with isolated symptoms of cystitis.

Common organisms: *Escherichia coli*, *Candida* spp (or yeast, not otherwise specified), *Enterococcus* spp, *Pseudomonas aeruginosa*, *Klebsiella* spp

Empiric therapy:

1. Remove urinary catheter.
2. Manage according to presenting symptoms, risk factors for resistant infection,* and antibiotic allergies:
   - Systemic symptoms
     - See *Complicated Urinary Tract Infections (Pyelonephritis)* for antibiotic therapy
     - If *Candida* spp suspected: Fluconazole (Diflucan®) 200 mg to 400 mg# by mouth daily for 14 days
   - Symptoms confined to lower urinary tract

○ See *Uncomplicated Urinary Tract Infections (Cystitis)* for antibiotic therapy ○ If *Candida* spp is suspected: Fluconazole (Diflucan®) 200 mg# by mouth daily for 14 days
*Antimicrobial resistance is highly prevalent in catheter-associated UTIs.

Community-Acquired Pneumonia (CAP) in Outpatient Setting[26,27]

Symptoms: Clinical features include fever, dyspnea, cough, and sputum production. Because these features alone are nonspecific, the official diagnosis of CAP requires an infiltrate on chest imaging.[22]

Common organisms: *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Mycoplasma pneumoniae, Staphylococcus aureus, Legionella species, Chlamydia pneumoniae, and Moraxella catarrhalis*[20,22]

NOTE: Bacteria associated with community-acquired cases of aspiration pneumonia are commonly *Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae*, and *Enterobacteriaceae*[23]

Empiric therapy:

Indication 1: Previously healthy patients without comorbidities and without risk factors for *Pseudomonas aeruginosa* or methicillin-resistant *Staphylococcus aureus* infection (e.g., prior respiratory infection with one of these organisms or hospitalization and receipt of parenteral antibiotics within the 90 days prior):

- Choose one of the five regimens below for a duration of 5 to 7 days:
    1. Amoxicillin (Amoxil®) 1 gram by mouth three times daily
    2. Azithromycin (Zithromax®) 500 mg x 1, then 250 mg by mouth once daily
    3. Clarithromycin (Biaxin®) 500 mg# by mouth twice daily
    4. Clarithromycin (Biaxin®) 1,000 mg# by mouth daily (extended-release)
    5. Doxycycline 100 mg by mouth twice daily

Indication 2: Major comorbidities (including chronic heart, renal, or liver disease, diabetes mellitus, asplenia, and immunosuppression), recent antibiotic use, age ≥ 65 years, smoking, alcohol dependence.

- Choose one of the two regimens below for a duration of 5 to 7 days:
    1. Select one extended-spectrum beta-lactam PLUS one macrolide OR doxycycline
        - Select one extended-spectrum beta-lactam (includes 3rd generation cephalosporins):
            - Amoxicillin-clavulanate (Augmentin®) 500 mg-125 mg# by mouth three times daily
            - Amoxicillin-clavulanate (Augmentin®) 875 mg-125 mg# by mouth twice daily
            - Cefpodoxime (Vantin®) 200 mg# by mouth twice daily
            - Cefuroxime (Ceftin®) 500 mg# by mouth twice daily
        - Select one macrolide or doxycycline:
            - Azithromycin (Zithromax®) 500 mg x 1 dose, then 250 mg by mouth once daily
            - Clarithromycin (Biaxin®) 500 mg by mouth twice daily
            - Clarithromycin (Biaxin®) 1,000 mg by mouth once daily (extended-release)
            - Doxycycline 100 mg by mouth twice daily
    2. Select one - monotherapy with a respiratory quinolone

- Levofloxacin (Levaquin®) 750 mg# by mouth daily
- Moxifloxacin (Avelox®) 400 mg# by mouth once daily

Indication 3: Aspiration pneumonia suspected based on witnessed aspiration event, imaging, risk factors for swallowing difficulties (neurologic, muscular, recent surgery), altered consciousness (drug or alcohol use, neurologic disease, seizure, anesthesia) and signs of pneumonia (fever, shortness of breath, purulent sputum, hypoxemia).[27,29]

- Choose one of the four regimens below for a duration of 5 days
  1. Amoxicillin-clavulanate (Augmentin®) 875 mg-125 mg# by mouth twice daily
  2. Amoxicillin-clavulanate extended-release (Augmentin® XR) 2000 mg-125 mg# by mouth twice daily
  3. Moxifloxacin (Avelox®) 400 mg# by mouth once daily
  4. Clindamycin (Cleocin®) 300 mg or 400 mg by mouth every 8 hours (less preferred therapy - carries a greater risk of *Clostridioides difficile* infection)

Dose requires adjustment for renal insufficiency.[20,21]

Best Practices For Antibiotic Use

1. **Thoughtful Decision-Making**

   Carefully consider antibiotic prescriptions based on individual patient circumstances including the type of infection, patient's goals of care, and prognosis. Restrict antibiotic use for patients with comfort-focused goals and a prognosis of weeks or less, except for specific conditions where symptom relief is achievable with antibiotics.

2. **Antibiotic Stewardship**

   Antibiotic stewardship is the effort to measure and improve how antibiotics are prescribed by clinicians and used by patients.[30] Implementing antibiotic stewardship in a hospice model may seem daunting. However, simply adapting a few key principles will ensure patient safety, symptom control, and minimize unnecessary use of antibiotics, decreasing cost and mitigating adverse effect outcomes. Key principles include:[31]

   - **Track antibiotic use** by medication, indication, and care team and regularly assess trends with the interdisciplinary team.
   - **Educate clinicians** on empiric antibiotic choice and dose recommendations when use is needed. (See *Empiric Therapy*)
   - **Prepare clinicians** with talking points for patient and caregiver conversations on adverse effects and when antibiotic use is no longer necessary for symptom control. (See *REMAP*)

3. **Further Research**

   Emphasize the need for more studies to guide antibiotic use in hospice care.

Related Palliative Pearls Content

- Palliative Management of Bacterial Infections
- Back to Basics: Skin Conditions & Topical Treatment
- *Clostridioides Difficile* Infection: Risks, Prevention & Medication Therapy

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