COP-005

Complicated UTI in Real Time

Copient AI for CME Outfitters

Learner Handouts — Combined Set

All seven post-module documents in one file · Current as of August 20, 2026

1. **Module 1 — Micro Report (Full Culture & Susceptibility)**
   Released after Module 1 — states the classification, preferred agents, and duration.
2. **Module 1 — Empiric Algorithm**
   Worked solution for the Module 1 case.
3. **Module 1 — Algorithm Quick Reference**
   Worked solution, condensed.
4. **Module 2 — Empiric Algorithm**
   Works the case through to ertapenem.
5. **Module 2 — Algorithm Quick Reference**
   Same, condensed.
6. **Module 3 — Empiric Algorithm**
   Names the step-down agent, dose, and duration.
7. **Module 3 — Algorithm Quick Reference**
   Same, condensed.

Each document below is separated by a labeled divider page. These are the documents released to learners after each module; in-conversation documents (point-of-care summary, micro reports for Modules 2 and 3, framework card) are served inside the Copient platform and are not part of this set.

SIMULATED EDUCATIONAL CONTENT — FOR CME/CE USE ONLY

DOCUMENT 1 OF 7

MODULE 1

Micro Report

Full Culture & Susceptibility · Released after Module 1

Urine Culture & Susceptibility Report — Final

Localized cUTI · No sepsis criteria · Outpatient

Case Context

63-year-old female · Type 2 diabetes (A1c 7.4%, well-controlled) · Recurrent UTI (4 episodes in past 2 years) · Post-menopausal

Chief complaint: Dysuria and urinary frequency × 2 days. Requesting "strong antibiotics" — has a wedding in two days.

TEMP	HR	BP	RR / SpO_2	WBC	CRP	CR / eGFR	DISPOSITION
37.0 °C	**78**	**122/74**	**16 / 98%**	**8,400/µL**	**14 mg/L**	**0.82 / >60**	**Outpatient**

- **Absence of systemic signs:** no fever, chills, rigors, flank pain, CVA tenderness, or confusion/altered mental status
- **Point-of-care urinalysis:** positive LE, positive nitrite, WBC 2+, moderate bacteria, no RBC, no casts
- **Blood cultures:** not indicated — no systemic signs or sepsis criteria

IDSA 2025 Classification — Localized vs. Systemic

The 2025 IDSA and EAU guidelines replace the traditional "complicated vs. uncomplicated" binary with a presentation-based classification.

Clinical Feature	This Patient	Systemic cUTI — Red Flags
Temperature	Afebrile (37.0 °C)	>38 °C / hypothermia
Blood pressure	Normotensive (122/74)	Hypotension / MAP <65
Heart rate	78 — normal	>100 (tachycardia)
Flank pain	None	Present — suggests pyelonephritis
Confusion / AMS	None	Present — consider sepsis
Rigors / chills	None	Present
Urinary symptoms	Dysuria, frequency	Dysuria, frequency (may also be present)
IDSA 2025 classification	Localized (bladder-confined)	Systemic (beyond bladder)
Site of care	Outpatient	Inpatient evaluation warranted
IV antibiotics	Not indicated	May be required

Teaching note. Diabetes alone is no longer sufficient to define complication status under the IDSA 2025 classification. This patient's diabetes is a risk factor for recurrence and treatment failure — but her presentation is localized, her vitals are stable, and she does not meet systemic or sepsis criteria. The appropriate classification is localized cUTI, and the appropriate setting is outpatient.

Culture Result — Final

Escherichia coli

Colony count >100,000 CFU/mL · Single organism · No contaminants · MALDI-TOF MS 99.8%

No ESBL detected · No carbapenemase detected · Susceptible profile — see panel below

Antimicrobial Susceptibility Panel

Broth microdilution unless otherwise noted · CLSI M100 breakpoints

Agent	MIC (µg/mL)	Breakpoint	Result
Penicillins & Combinations			
Ampicillin	>32	S ≤8	**R**
Amoxicillin-clavulanate	8	S ≤8	**S**
Cephalosporins			
Cephalexin	8	S ≤16	**S**
Cefdinir	1	S ≤1	**S**
Ceftriaxone	0.5	S ≤1	**S**
Fluoroquinolones			
Ciprofloxacin †	>4	S ≤0.25	**R**
Levofloxacin †	>8	S ≤0.5	**R**
Folate Pathway Inhibitors			
Trimethoprim-sulfamethoxazole †	>4/76	S ≤2/38	**R**
Miscellaneous			

Nitrofurantoin ‡	32	S ≤32	**S**
Fosfomycin (oral) ‡ §	32	S ≤64	**S**
Gentamicin	1	S ≤4	**S**

Susceptibility Interpretation Notes

† Ciprofloxacin, levofloxacin, trimethoprim-sulfamethoxazole. All three are resistant. Fluoroquinolone resistance is increasingly common in community-acquired *E. coli* UTI, particularly in patients with recurrent UTIs and prior antibiotic exposure. This isolate's resistance pattern is consistent with prior treatment history. Neither agent class should be prescribed for this patient.

‡ Nitrofurantoin and fosfomycin (oral). Both are susceptible and are appropriate options for localized cUTI confined to the bladder. Scope note: neither nitrofurantoin nor oral fosfomycin achieves adequate renal parenchymal concentrations, and neither should be used if the presentation were systemic (pyelonephritis). They are appropriate here because the classification is localized.

§ Fosfomycin (oral). Tested by agar dilution; CLSI fosfomycin breakpoints are established for *Escherichia coli* urinary isolates only.

◆ No ESBL, carbapenemase, or MDR resistance detected. This isolate does not carry extended-spectrum beta-lactamases and is susceptible to multiple agents. Broad-spectrum or IV therapy is not indicated for this localized presentation.

Stewardship Note — Resisting Over-Treatment Pressure

Patient request context. This patient is requesting "strong antibiotics" ahead of a social event. "Strong" in this context likely means broader-spectrum or IV therapy — neither of which is clinically indicated for a localized cUTI with a susceptible organism. The role of the clinician is to align treatment with evidence, not patient preference for broader coverage.

Appropriate agent selection. Nitrofurantoin (5-day course) or oral fosfomycin (single dose) are first-line evidence-based options for localized cUTI caused by susceptible *E. coli* per IDSA 2025 cUTI guideline. Amoxicillin-clavulanate or an oral cephalosporin (cephalexin, cefdinir) are acceptable alternatives.

What not to prescribe. Fluoroquinolones (resistant; also reserved for more complex indications), trimethoprim-sulfamethoxazole (resistant), or IV antibiotics (no systemic signs — IV therapy adds cost, risk, and healthcare resource burden with no clinical benefit for this presentation).

Treatment duration. Per IDSA 2025 duration guideline, shorter courses (5–7 days for most localized cUTI) are appropriate and non-inferior to longer courses. A 14-day course is not indicated.

Diabetes as a comorbidity. Diabetes increases recurrence risk and may influence follow-up planning, but does not change the treatment approach for this localized presentation and does not mandate admission or IV therapy under the 2025 IDSA classification.

Interpretive Comment

***E. coli* localized cUTI — outpatient presentation, susceptible isolate.** This isolate is susceptible to multiple oral agents including nitrofurantoin, oral fosfomycin, and oral beta-lactams. The resistance to fluoroquinolones and trimethoprim-sulfamethoxazole is clinically important but does not require escalation to broader-spectrum or IV therapy, as multiple appropriate oral alternatives remain available.

Classification confirmation. This patient's presentation meets criteria for localized cUTI under the IDSA 2025 classification — dysuria and frequency without fever, rigors, flank pain, or systemic signs. She does not meet criteria for systemic cUTI or pyelonephritis. Outpatient management with an appropriate oral agent is the evidence-based course of action.

Recurrence risk factors. Recurrent UTI history, post-menopausal status, and diabetes are all established risk factors for recurrence. A conversation about recurrence prevention strategies (vaginal estrogen, behavioral modifications, potential prophylaxis) is appropriate at this visit, separate from the acute treatment decision.

Follow-up. Routine test-of-cure is not recommended after treatment of localized cUTI in the absence of persistent symptoms. Advise the patient to return if symptoms do not improve within 48–72 hours or if fever, chills, or flank pain develop — which would indicate progression to systemic involvement requiring reassessment.

DOCUMENT 2 OF 7

MODULE 1

Empiric Algorithm

Worked solution for the Module 1 case

Four-Step Empiric Therapy Algorithm

Worked Solution — Module 1

2025 IDSA/EAU four-step empiric therapy algorithm. This algorithm is available as an optional reference. Work through each step against the patient's findings before making a treatment decision.

Patient: 63-year-old woman · Dysuria, urinary frequency · Afebrile · Normotensive · No flank pain · Diabetes · Recurrent UTI

1 Assess Severity of Illness

Is there evidence of sepsis or systemic involvement? Look for fever, hypotension, tachycardia, altered mental status, rigors, and flank pain.

Temperature: T 37.0 °C — afebrile. No fever.
Blood pressure: BP 122/74 mmHg — normotensive. No hypotension.
Heart rate: HR 78 — no tachycardia.
Flank pain / CVA tenderness: None.
Altered mental status / rigors: None.
Sepsis criteria (SIRS/qSOFA): Not met — no systemic involvement.
IDSA 2025 classification: LOCALIZED — symptoms confined to the bladder. Not systemic.

Decision: Severity LOW. Localized presentation, no sepsis. Outpatient management appropriate — no IV antibiotics indicated.

2 Evaluate Resistance Risk Factors

Consider prior antibiotic exposure, prior urine cultures, travel history, healthcare exposure, and local resistance patterns.

Prior antibiotic exposure: Nitrofurantoin × 7 days, 6 months prior. No recent fluoroquinolone or broad-spectrum exposure.
Prior urine culture: Last culture 4 months ago: *E. coli*, susceptible to nitrofurantoin and fosfomycin.
Travel history: No recent international travel.
Healthcare exposure: Outpatient only — no recent hospitalization or procedures.
ESBL / MDR risk: Low — no risk factors for ESBL-producing organisms.
Fluoroquinolone resistance risk: Moderate to high — recurrent UTI with prior antibiotic exposure. Confirmed resistant on this culture.
Trimethoprim-sulfamethoxazole: Confirmed resistant on this culture — not appropriate.

Decision: Fluoroquinolone-resistant, trimethoprim-sulfamethoxazole-resistant *E. coli*. Nitrofurantoin and fosfomycin susceptible. No ESBL — narrow-spectrum oral therapy appropriate.

3 Consider Patient-Specific Factors

Allergies, comorbidities, renal function, adherence, and patient preferences — including requests that may not align with evidence.

Allergies: None documented.
Type 2 diabetes: Well controlled (A1c 7.4%). Does not change agent selection for localized cUTI under IDSA 2025. May increase recurrence risk — address at follow-up.
Renal function: Creatinine 0.82 mg/dL, eGFR >60 — nitrofurantoin appropriate (requires eGFR ≥30).
Adherence and convenience: Single-dose fosfomycin offers a one-time oral option — may suit the patient's schedule.
Request for 'strong antibiotics': Clinically unwarranted. Broader-spectrum or IV therapy adds risk and cost with no benefit for this localized, susceptible presentation. Address expectations with shared decision-making.
Recurrence history: 4 episodes in 2 years. Discuss prevention (vaginal estrogen, behavioral strategies, possible prophylaxis) separately from acute treatment.

Decision: No contraindications to narrow-spectrum oral therapy. Single-dose fosfomycin or 5-day nitrofurantoin are first-line per IDSA 2025.

4 Use Local Antibiogram

For localized cUTI the individual culture result is the primary guide; local antibiogram data confirms which agents remain reliably active in the community.

Relevance here: For this localized presentation the culture result leads. Local antibiogram matters most for empiric therapy in systemic or septic cases.
Nitrofurantoin: Typically <5% resistance in community *E. coli* — a reliable empiric choice for localized cUTI at most institutions.
Fosfomycin: Typically <5% for *E. coli* causing cystitis — reliable empiric option.
Fluoroquinolones: Community *E. coli* resistance often exceeds 20–30% in many US regions, consistent with this isolate. Not recommended empirically.
Trimethoprim-sulfamethoxazole: Commonly exceeds 20% in recurrent UTI patients with prior exposure — not recommended empirically without confirmed susceptibility.

Decision: Nitrofurantoin or fosfomycin as empiric first-line. Culture confirms susceptibility — proceed with targeted narrow-spectrum oral therapy.

Treatment Decision Summary

Classification	Localized cUTI (IDSA 2025) — bladder-confined, no systemic signs
Site of care	Outpatient — no admission or IV therapy indicated
Preferred agents	Nitrofurantoin 100 mg ER PO BID × 5 days, or fosfomycin 3 g PO single dose
Alternatives	Amoxicillin-clavulanate PO, cephalexin PO, or cefdinir PO (culture-guided)
Duration	5–7 days. A 14-day course is not indicated

DO NOT USE: Fluoroquinolones (resistant) · Trimethoprim-sulfamethoxazole (resistant) · IV antibiotics (no systemic indication) · Extended duration beyond 7 days (non-inferior to shorter courses per IDSA 2025)

KEY TEACHING POINTS — MODULE 1

- The IDSA 2025 guideline replaces the 'complicated versus uncomplicated' binary with presentation-based classification. This patient has diabetes, but diabetes alone no longer defines complicated status — her presentation is localized because she has no systemic signs.
- Step 1 is the critical decision fork. If this patient had fever, rigors, or flank pain, the classification would be systemic and the entire algorithm — agent, route, and site of care — would change.
- Broader-spectrum or IV antibiotics are not 'stronger' in the sense of clinical efficacy for a localized susceptible infection. They carry greater side-effect risk, drive resistance, and cost more. Shared decision-making should focus on why the targeted narrow-spectrum agent is right.
- Nitrofurantoin and oral fosfomycin would NOT be appropriate if the presentation were systemic — they do not reach adequate renal parenchymal concentrations. This is how classification directly drives agent selection.

MODULE 1

Algorithm Quick Reference

Worked solution, condensed

Four-Step Algorithm — Quick Reference

One-Page Summary — Module 1

Patient: 63-year-old woman · Dysuria, urinary frequency · Afebrile · Normotensive · No flank pain · Diabetes · Recurrent UTI

1 Assess Severity — Localized or systemic?

Findings: T 37.0 °C · HR 78 · BP 122/74 · no rigors · no flank pain · no altered mental status · afebrile and normotensive

Decision: LOW severity — localized cUTI. No sepsis criteria met.

2 Assess Resistance Risk — How likely is a resistant organism?

Findings: Recurrent UTI · prior nitrofurantoin · no recent fluoroquinolone or broad-spectrum exposure · no travel · no ESBL risk factors

Decision: Low MDR risk. No ESBL concern.

3 Consider Patient Factors — What can this patient receive and take?

Findings: No allergies · eGFR >60 (nitrofurantoin acceptable) · diabetes is a recurrence risk, not an admission indication · patient preference is not a clinical indication

Decision: No contraindications to narrow-spectrum oral therapy.

4 Use Local Antibiogram — What does local data support?

Findings: Fluoroquinolone resistance >20–30% nationally, consistent with this isolate · nitrofurantoin <5% resistance · fosfomycin <5% resistance

Decision: Nitrofurantoin or fosfomycin confirmed first-line.

Treatment Decision Summary

Classification	Localized cUTI (IDSA 2025) — bladder-confined, no systemic signs
Site of care	Outpatient — no admission or IV therapy indicated
Preferred agents	Nitrofurantoin 100 mg ER PO BID × 5 days, or fosfomycin 3 g PO single dose
Alternatives	Amoxicillin-clavulanate PO, cephalexin PO, or cefdinir PO (culture-guided)
Duration	5–7 days. A 14-day course is not indicated

Watch Out For

- Diabetes alone does not define systemic cUTI under IDSA 2025 — classification is presentation-based. This patient is localized.
- 'Strong antibiotics' does not mean broader spectrum for a localized susceptible infection. Targeted narrow-spectrum therapy is the right choice.
- Nitrofurantoin and fosfomycin are bladder-only agents — do NOT use them if the presentation were systemic (pyelonephritis).

DO NOT USE: Fluoroquinolones (resistant) · Trimethoprim-sulfamethoxazole (resistant) · IV antibiotics (no systemic indication) · Extended duration beyond 7 days (non-inferior to shorter courses per IDSA 2025)

DOCUMENT 4 OF 7

MODULE 2

Empiric Algorithm

Works the case through to ertapenem

Four-Step Empiric Therapy Algorithm

Worked Solution — Module 2

2025 IDSA/EAU four-step empiric therapy algorithm. This algorithm is available as an optional reference. Work through each step against the patient's findings before making a treatment decision.

Patient: 70-year-old man · Fever, rigors, urinary hesitancy · Hypotension (fluid-responsive) · Recent travel to Southern Europe · Recent fluoroquinolone exposure · BPH

1 Assess Severity of Illness

Is there evidence of sepsis or systemic involvement? Evaluate for organ dysfunction, hemodynamic instability, and systemic inflammatory response.

Temperature: T 38.9 °C — fever present.
Blood pressure: 94/58 mmHg on arrival — hypotension. Improved to 102/66 after 1 L normal saline; fluid-responsive, but hypotension was present.
Heart rate: HR 108 — tachycardia present.
Respiratory rate / SpO_2: RR 22, SpO_2 96% — mildly elevated respiratory rate.
Altered mental status: Confusion noted by family — possible sepsis-associated encephalopathy.
Lactate: 2.1 mmol/L — elevated, trending down after fluids.
Blood cultures: 2/2 bottles positive, gram-negative rods preliminary — bacteremia present.
IDSA 2025 classification: SYSTEMIC — fever, rigors, hypotension, tachycardia, bacteremia. Meets sepsis criteria.

Decision: Severity HIGH. Systemic cUTI with sepsis and bacteremia. Inpatient admission required, IV antibiotics indicated. Start empiric therapy promptly — do not wait for culture results.

2 Evaluate Resistance Risk Factors

Identify risk factors for resistant organisms — particularly ESBL-producing Enterobacterales — to guide empiric agent selection.

Recent antibiotic exposure: Ciprofloxacin 500 mg PO BID × 5 days, completed about 3 weeks prior. Prior fluoroquinolone exposure is a strong predictor of fluoroquinolone-resistant and ESBL-producing organisms.
Recent travel: Returned from Southern Europe (Spain) within the past 4 weeks. Southern Europe and the Middle East have high community-acquired ESBL prevalence in urinary Enterobacterales.
Prior urine culture: None available at presentation. Treat as ESBL-risk until proven otherwise.
Healthcare exposure: Outpatient only — no recent hospitalization or urologic procedures. Travel plus fluoroquinolone exposure is sufficient on its own.
BPH: Increases risk of incomplete bladder emptying and recurrent UTI but does not independently raise ESBL risk.
ESBL risk assessment: HIGH — two independent risk factors present.

Decision: Resistance risk HIGH for an ESBL-producing organism. Empiric carbapenem coverage is warranted; do not rely on cephalosporins or fluoroquinolones empirically.

3 Consider Patient-Specific Factors

Allergies, comorbidities, organ function, and individual factors that may influence agent selection or dosing.

Allergies: None documented.
Renal function: Creatinine 1.38 mg/dL — mildly elevated, likely acute kidney injury in the setting of sepsis. Carbapenem dosing should account for renal function; monitor during admission.
BPH: On tamsulosin — a structural urinary tract factor. Consider urology consult if the patient does not respond as expected; obstruction may complicate resolution.
Age 70: Increased risk of adverse drug events. Avoid aminoglycosides as primary therapy given renal function.
Aminoglycosides: Gentamicin is susceptible on culture, and aminoglycosides are alternative agents for ESBL-E pyelonephritis per IDSA 2024 AMR Guidance — but not preferred here given renal function and age.
IV fosfomycin (Contepo): FDA-approved October 2025 for cUTI including acute pyelonephritis. Susceptibility expected; MIC testing not performed on this panel. Consult ID or pharmacy if a carbapenem-sparing approach is desired.

Decision: No allergies. Mild acute kidney injury — monitor renal function. BPH warrants follow-up if response is suboptimal. Carbapenem appropriate and safe; adjust dose for renal function.

4 Use Local Antibiogram

For systemic and septic presentations, local antibiogram data is essential for empiric carbapenem selection and to guide de-escalation planning.

Ertapenem: Active against ESBL-producing *E. coli* and *K. pneumoniae*. Does not cover *P. aeruginosa* or *Enterococcus* — appropriate for community-acquired ESBL-E without Pseudomonas risk.
Meropenem / imipenem-cilastatin: Group 2 carbapenems, broader spectrum including Pseudomonas. Reserve for documented Pseudomonas risk or institutional protocols favoring broader empiric coverage in sepsis.
Piperacillin-tazobactam: Carbapenems are preferred for ESBL-E pyelonephritis and cUTI. IDSA 2024 AMR Guidance is more permissive here than for non-urinary ESBL infections — it acknowledges piperacillin-tazobactam may be reasonable for cUTI specifically, though outcomes modestly favor carbapenems.
Local ESBL prevalence: Check the institutional antibiogram for community-acquired *E. coli* ESBL rates. In high-prevalence settings (>20%), empiric carbapenem for septic presentations is standard practice.
De-escalation trigger: Once cultures confirm susceptibility and the patient is clinically stable — afebrile ≥48 hours, improving labs, blood cultures cleared — consider de-escalation and IV-to-oral transition.

Decision: Ertapenem is the appropriate empiric choice for community-acquired ESBL-E septic cUTI. Begin ertapenem now; revisit for de-escalation at 48–72 hours.

Treatment Decision Summary

Classification	Systemic cUTI with sepsis and bacteremia (IDSA 2025) — inpatient
Site of care	Inpatient admission — IV antibiotics, monitoring, and blood culture follow-up required
Empiric therapy	Ertapenem 1 g IV q24h, or meropenem 1 g IV q8h if Pseudomonas risk is present
Duration	7 days total (IV plus oral) for most systemic cUTI; 10 days in select cases, per IDSA 2025
Oral step-down	Once stable and blood cultures cleared: oral fosfomycin 3 g q48h for ESBL *E. coli*, or tebipenem pivoxil 600 mg q6h. Not for initial therapy

DO NOT USE: Fluoroquinolones (resistant) · Trimethoprim-sulfamethoxazole (resistant) · Piperacillin-tazobactam (ESBL cUTI — carbapenems preferred; IDSA 2024 AMR Guidance considers it a reasonable alternative) · Cephalosporins (ESBL — presumed resistant) · Oral agents as initial therapy in a septic presentation

KEY TEACHING POINTS — MODULE 2

- Step 1 is the fork that changes everything. Once systemic involvement and sepsis are confirmed, the whole framework shifts — IV therapy, inpatient admission, blood cultures, and broad empiric coverage all follow.
- Step 2 is where the ESBL decision lives. Two independent risk factors — recent fluoroquinolone exposure and travel to Southern Europe — together create high ESBL probability. Either alone would warrant consideration; both together make empiric carbapenem the standard approach.
- Carbapenems remain preferred for ESBL-E pyelonephritis. IDSA 2024 AMR Guidance is more permissive here than for non-urinary ESBL infections — it acknowledges piperacillin-tazobactam may be reasonable for cUTI specifically, even though outcomes modestly favor carbapenems.
- De-escalation is part of stewardship. Once the patient stabilizes and culture data confirm susceptibility, re-apply the algorithm to decide whether a narrower agent or oral transition is appropriate. Carbapenem therapy should not continue indefinitely if a safer, narrower option exists.
- Newer agents and evolving step-down options: cefepime-enmetazobactam (Exblifep, February 2024) and IV fosfomycin (Contepo, October 2025) are carbapenem-sparing IV options. For oral step-down, oral fosfomycin trometamol at q48h dosing is supported by RCT evidence once the patient has stabilized on IV carbapenem (Angkanavisan et al., Int J Infect Dis 2026), and tebipenem pivoxil (Utebzi, June 2026) is an additional option whose FDA indication explicitly includes *E. coli*.

MODULE 2

Algorithm Quick Reference

Same, condensed

Four-Step Algorithm — Quick Reference

One-Page Summary — Module 2

Patient: 70-year-old man · Fever, rigors, urinary hesitancy · Hypotension (fluid-responsive) · Recent travel to Southern Europe · Recent fluoroquinolone exposure · BPH

1 Assess Severity — Localized or systemic?

Findings: T 38.9 °C · HR 108 · BP 94/58 (fluid-responsive) · lactate 2.1 · blood cultures 2/2 positive · confusion

Decision: HIGH — systemic cUTI with sepsis and bacteremia. Admit. IV now.

2 Assess Resistance Risk — How likely is a resistant organism?

Findings: Fluoroquinolone exposure 3 weeks prior, plus travel to Southern Europe (high ESBL prevalence) — two independent ESBL risk factors. No prior culture.

Decision: HIGH ESBL risk. Empiric carbapenem required.

3 Consider Patient Factors — What can this patient receive and take?

Findings: No allergies · creatinine 1.38 (mild acute kidney injury — monitor) · age 70, so avoid aminoglycosides as primary therapy · BPH, so urology consult if no response

Decision: Carbapenem appropriate. Adjust dose for renal function.

4 Use Local Antibiogram — What does local data support?

Findings: Ertapenem covers ESBL-E and there are no Pseudomonas risk factors, so a Group 1 carbapenem is sufficient. Reassess at 48–72 hours for de-escalation.

Decision: Ertapenem 1 g IV q24h. De-escalate once cultures confirm.

Treatment Decision Summary

Classification	Systemic cUTI with sepsis and bacteremia (IDSA 2025) — inpatient
Site of care	Inpatient admission — IV antibiotics, monitoring, and blood culture follow-up required
Empiric therapy	Ertapenem 1 g IV q24h, or meropenem 1 g IV q8h if Pseudomonas risk is present
Duration	7 days total (IV plus oral) for most systemic cUTI; 10 days in select cases, per IDSA 2025
Oral step-down	Once stable and blood cultures cleared: oral fosfomycin 3 g q48h for ESBL *E. coli*, or tebipenem pivoxil 600 mg q6h. Not for initial therapy

Watch Out For

- Carbapenems remain preferred for ESBL-E pyelonephritis. IDSA 2024 AMR Guidance is more permissive here than for non-urinary ESBL infections — it acknowledges piperacillin-tazobactam may be reasonable for cUTI specifically, even though outcomes modestly favor carbapenems.
- Oral fosfomycin (3 g q48h) is a carbapenem-sparing step-down for ESBL *E. coli*, once bacteremia clears and the patient is stable. Not initial therapy. Not for Klebsiella (intrinsic *fosA* resistance).
- Tebipenem pivoxil (Utebzi, June 2026) is an oral carbapenem whose FDA indication explicitly includes *E. coli* — an alternative step-down via susceptibility inference.
- Confirm blood cultures have cleared before any oral step-down — bacteremia was an exclusion criterion in the fosfomycin step-down trial (Angkanavisan 2026).

DO NOT USE: Fluoroquinolones (resistant) · Trimethoprim-sulfamethoxazole (resistant) · Piperacillin-tazobactam (ESBL cUTI — carbapenems preferred; IDSA 2024 AMR Guidance considers it a reasonable alternative) · Cephalosporins (ESBL — presumed resistant) · Oral agents as initial therapy in a septic presentation

MODULE 3

Empiric Algorithm

Names the step-down agent, dose, and duration

Four-Step Framework at Transition of Care

Worked Solution — Module 3

2025 IDSA/EAU four-step framework, re-applied at the transition-of-care decision point. The question is no longer what empiric therapy to start, but whether and how to step down.

Patient: 60-year-old woman · Inpatient day 3 · ESBL *Klebsiella pneumoniae* pyelonephritis · Clinically stable · Afebrile ≥24 hours · Negative imaging · Fluoroquinolone allergy · Lives alone

1 Reassess Severity of Illness

Has the patient's clinical status changed? Re-evaluate severity and confirm resolution of systemic signs before considering step-down.

Temperature (day 3): 37.1 °C — afebrile for ≥24 hours.
Blood pressure: 128/78 — normotensive, stable.
Heart rate: 74 — normal sinus rhythm.
Inflammatory markers: WBC 9,200/µL, down from 16,200. CRP 44 mg/L, down from 118.
Oral intake: Tolerating soft diet — adequate for oral antibiotic absorption.
Blood cultures: 2/2 bottles negative at day 3 — bacteremia has cleared.
Imaging: CT at admission showed no obstruction, abscess, or nephrolithiasis — no structural complication requiring intervention.

Decision: Systemic signs resolved. The patient is stable and responding to therapy. IV-to-oral transition is clinically appropriate.

2 Re-evaluate Resistance Risk for Oral Step-Down

What oral agents are available for ESBL-producing Klebsiella pneumoniae? This is where the oral step-down challenge becomes apparent.

ESBL *K. pneumoniae*: Susceptible to IV carbapenems. Resistant to fluoroquinolones, trimethoprim-sulfamethoxazole, and cephalosporins.
Fluoroquinolone allergy: Documented rash — contraindicated regardless of susceptibility.
Trimethoprim-sulfamethoxazole: Resistant on culture.
Oral cephalosporins: Cephalexin, cefdinir and cefuroxime all resistant on culture.
Nitrofurantoin: Resistant on culture, and it does not achieve adequate renal parenchymal concentrations for pyelonephritis. Not appropriate regardless of MIC.
Oral fosfomycin: *K. pneumoniae* carries a chromosomal *fosA* gene encoding a fosfomycin-modifying enzyme that confers intrinsic resistance — a class effect. Should not be used for this organism regardless of in vitro MIC. This is the clinically important distinction from ESBL *E. coli*, where oral fosfomycin may be a carbapenem-sparing step-down (Angkanavisan et al., Int J Infect Dis 2026).
Standard oral panel gap: No conventional oral agent on the standard susceptibility panel is appropriate for this organism in this indication.
Susceptibility inference: Tebipenem pivoxil, an oral carbapenem FDA-approved June 2026, is not on the standard panel, but susceptibility is inferred from confirmed carbapenem susceptibility and known class activity. Its approved indication explicitly includes *Klebsiella pneumoniae* — a critical distinction from oral fosfomycin, whose CLSI breakpoints are validated for *E. coli* urinary isolates only.

Decision: Standard oral options are all excluded. An oral carbapenem (tebipenem pivoxil) is the appropriate step-down agent, with susceptibility inferred from mechanism rather than reported on the panel.

3 Consider Patient-Specific Factors for Discharge

Patient factors matter most at the transition-of-care decision point — adherence, social situation, and safety-net planning are all in play.

Fluoroquinolone allergy: Documented — eliminates a major oral step-down option that would otherwise be available.
Lives alone: High-risk social factor for adherence and safety. Structured discharge instructions, a caregiver check-in, and clear escalation criteria are required.
Recurrent UTI history: 3 episodes in 18 months — elevated recurrence risk. Address prevention at discharge (vaginal estrogen, behavioral modification, possible prophylaxis referral).
Tebipenem dosing: 600 mg PO q6h — four times daily. Adherence counseling is essential: alarm reminders, dosing with or without food, and consequences of missed doses.
Carnitine warning: Tebipenem pivoxil should not be used in patients with primary or secondary carnitine deficiency. Confirm before prescribing.
Oral intake: Tolerating soft diet — IV-to-oral transition is physiologically appropriate.

Decision: QID dosing requires adherence counseling. Because she lives alone, a structured discharge plan, red-flag symptoms, and a 7–14 day follow-up appointment are required before discharge.

4 Apply Guidelines — Duration, Transition Timing, and Follow-Up

For the IV-to-oral transition and discharge planning, IDSA 2025 recommendations on duration and transition timing apply directly.

Total duration: 7–10 days total (IV plus oral) per IDSA 2025 for systemic cUTI. With 3 days of IV completed, 4–7 additional days of oral therapy at discharge.
Transition timing: Clinical stability criteria met at day 3 — afebrile ≥24 hours, tolerating oral intake, negative blood cultures, improving labs. IDSA 2025 and supporting data (Veillette 2024; Sutton 2020) confirm oral step-down is appropriate and non-inferior at this stage.
Tebipenem dosing: 600 mg PO q6h × 4–7 days to complete the 7–10 day total course.
Test of cure: Routine test-of-cure urine culture is not recommended after treatment of systemic cUTI in the absence of persistent symptoms.
Follow-up: Within 7–14 days post-discharge. Review culture sensitivities, assess response, and address recurrence prevention.
Recurrence prevention: Topical vaginal estrogen reduces recurrence risk post-menopause. Consider ID or urology referral for a recurrent cUTI management plan.

Decision: Discharge on tebipenem pivoxil 600 mg PO q6h to complete a 7–10 day total course, with a structured discharge plan, adherence counseling, red-flag symptoms, and 7–14 day follow-up.

Treatment Decision Summary

Current status	Clinically stable — meets IV-to-oral transition criteria
Stop IV therapy	Discontinue ertapenem IV at day 3 — transition to oral
Oral step-down	Tebipenem pivoxil (Utebzi) 600 mg PO q6h × 4–7 days to complete a 7–10 day total course
Adherence counseling	QID dosing — alarm reminders, consistent timing, food interactions, what to do if a dose is missed
Discharge plan	Red-flag symptoms · culture result follow-up · 7–14 day follow-up appointment · recurrence prevention counseling

DO NOT USE: Fluoroquinolones (allergy and resistant) · Trimethoprim-sulfamethoxazole (resistant) · Oral cephalosporins (resistant) · Nitrofurantoin (resistant, and pyelonephritis scope limitation) · Oral fosfomycin (intrinsic *K. pneumoniae fosA* resistance — inappropriate regardless of MIC) · Continuing IV beyond clinical stability

KEY TEACHING POINTS — MODULE 3

- The four-step framework applies at transition of care, not just at initiation. Re-running the steps at day 3 is how clinicians make structured step-down decisions rather than defaulting to keeping the IV going because it is working.
- The core teaching challenge has two layers: susceptibility inference, since tebipenem pivoxil is not on the standard panel and requires reasoning from carbapenem class activity; and organism-specific fosfomycin exclusion, since *K. pneumoniae* carries intrinsic chromosomal *fosA*-mediated resistance and CLSI fosfomycin breakpoints are validated for *E. coli* urinary isolates only.
- The key contrast: for ESBL *E. coli*, oral fosfomycin may be a viable carbapenem-sparing step-down supported by RCT data; for ESBL *K. pneumoniae* it is not — and tebipenem pivoxil fills that gap precisely because its FDA-approved indication explicitly includes *Klebsiella pneumoniae*. The organism choice in this case was deliberate.
- Continuing IV therapy beyond clinical stability is not a neutral decision. It extends hospital stay, increases IV access complications, and prolongs exposure to the hospital environment.
- Living alone is not a reason to keep a patient in hospital — it is a reason to invest in a thorough discharge plan. The distinction matters for both stewardship and resource use.

MODULE 3

Algorithm Quick Reference

Same, condensed

Four-Step Algorithm — Quick Reference

One-Page Summary — Module 3

Patient: 60-year-old woman · Inpatient day 3 · ESBL *Klebsiella pneumoniae* pyelonephritis · Clinically stable · Afebrile ≥24 hours · Negative imaging · Fluoroquinolone allergy · Lives alone

1 Reassess Severity — Has the picture changed?

Findings: T 37.1 °C · HR 74 · BP 128/78 · WBC 9,200 (down from 16,200) · CRP 44 (down from 118) · tolerating oral intake · blood cultures negative · CT shows no obstruction, abscess or stones

Decision: Resolved and stable. IV-to-oral transition appropriate.

2 Re-evaluate Oral Step-Down — What is actually available?

Findings: ESBL *K. pneumoniae* — fluoroquinolone resistant plus allergy · trimethoprim-sulfamethoxazole resistant · oral cephalosporins resistant · nitrofurantoin resistant and scope-limited for pyelonephritis · fosfomycin RESISTANT (intrinsic *fosA*, a *K. pneumoniae* class effect) · tebipenem not reported on the panel, susceptibility inferred from carbapenem class activity, and the FDA indication includes *K. pneumoniae*

Decision: Fosfomycin excluded. Tebipenem is the only viable oral option.

3 Consider Patient Factors — What can she manage at home?

Findings: Fluoroquinolone allergy (documented rash) · lives alone, so adherence support is essential · tebipenem is QID dosing (600 mg q6h), so counseling is required · confirm no carnitine deficiency · tolerating oral intake

Decision: No contraindication to tebipenem. Discharge plan required.

4 Apply Guidelines — How long, and what next?

Findings: Day 3 of IV · IDSA 2025: 7–10 days total (IV plus oral), so 4–7 days oral at discharge · IV-to-oral transition at day 3 supported by IDSA 2025 and RCT data

Decision: Stop IV. Discharge on tebipenem 600 mg q6h × 4–7 days.

Treatment Decision Summary

Current status	Clinically stable — meets IV-to-oral transition criteria
Stop IV therapy	Discontinue ertapenem IV at day 3 — transition to oral
Oral step-down	Tebipenem pivoxil (Utebzi) 600 mg PO q6h × 4–7 days to complete a 7–10 day total course
Adherence counseling	QID dosing — alarm reminders, consistent timing, food interactions, what to do if a dose is missed
Discharge plan	Red-flag symptoms · culture result follow-up · 7–14 day follow-up appointment · recurrence prevention counseling

Watch Out For

- Fosfomycin is RESISTANT for *K. pneumoniae* — intrinsic chromosomal *fosA* enzyme, a class effect. Not appropriate regardless of MIC. Unlike ESBL *E. coli*, where fosfomycin step-down may be an option, *K. pneumoniae* eliminates it.
- Tebipenem pivoxil's FDA indication explicitly includes *Klebsiella pneumoniae* — distinguishing it from fosfomycin. Susceptibility is inferred, not reported on the standard panel.
- QID dosing is a real adherence barrier and the patient lives alone. Alarm reminders and written instructions are part of the prescribing decision.
- Continuing IV beyond day 3 in a stable patient adds length of stay, cost and IV access risk with no clinical benefit.

DO NOT USE: Fluoroquinolones (allergy and resistant) · Trimethoprim-sulfamethoxazole (resistant) · Oral cephalosporins (resistant) · Nitrofurantoin (resistant, and pyelonephritis scope limitation) · Oral fosfomycin (intrinsic *K. pneumoniae fosA* resistance — inappropriate regardless of MIC) · Continuing IV beyond clinical stability