



### Patient Scenario #1:

A 57-year-old man is admitted to a community hospital in rural Iowa following a motor vehicle accident. Emergency surgery is performed to control internal bleeding and the patient is stabilized while moved to the ICU and requiring mechanical ventilation. On post-op day 3, he develops fever and purulent sputum. A chest x-ray identifies a new pulmonary infiltrate in both lungs. A Gram stain of the sputum reveals high numbers of a Gram-negative rod. The hospital has a low rate of carbapenem resistance among Gram-negative pathogens, and has yet to identify an organism exhibiting metallo-beta-lactamase. The hospital data shows that approximately 28% of Enterobacterales and *P. aeruginosa* produce ESBLs. Culture and susceptibility results will be available in 48-72 hours. Which of the following would be the most appropriate initial antimicrobial agent?

- A. Piperacillin-tazobactam
- B. Imipenem-cilastatin
- C. Ceftazidime-avibactam
- D. Cefiderocol

### Patient Scenario #2:

Consider the same patient; however, now the scenario is occurring at a hospital in New York City where the rate of carbapenem resistance among Enterobacterales is 17%. There has also been a recent outbreak of NDM-1-producing *P. aeruginosa* in the ICU. Though the hospital has rapid diagnostics available, a backlog in the clinical microbiology lab will delay results for 12 hours. Which of the following would be the most appropriate initial antimicrobial agent?

- A. Piperacillin-tazobactam
- B. Imipenem-cilastatin
- C. Ceftazidime-avibactam
- D. Cefiderocol

### Points to Consider

- How does the local epidemiology affect treatment choices?
- How do the possible resistance mechanisms help guide antimicrobial selection?

# Answer Key

## Patient Scenario #1

**Answer:** B. Imipenem-cilastatin

**Explanation:**

In the rural community hospital, there is a low rate of carbapenem resistance and no report of MBLs, and so the initial use of antimicrobial agents that are designed to target these resistance mechanisms (i.e., ceftazidime-avibactam, cefiderocol) are not preferred. The presence of ESBLs can be a concern and so an agent with activity against ESBL-producing organisms would be appropriate. Based on the 2020 IDSA guidance on the treatment of multidrug-resistant Gram-negative infections, a carbapenem, such as imipenem-cilastatin, would be the most appropriate choice for treatment in this scenario. IDSA indicates that piperacillin-tazobactam should be avoided in ESBL-producing Enterobacterales infections, even if in vitro susceptibility to piperacillin-tazobactam is demonstrated. This is based on the results from the MERINO trial that demonstrated inferior outcomes with piperacillin-tazobactam compared with a carbapenem.

## Patient Scenario #2

**Answer:** D. Cefiderocol

**Explanation:**

In this scenario where the patient is admitted to an urban hospital with a significant presence of carbapenem-resistant Enterobacterales, antimicrobial agents with in vitro activity against these pathogens should be initially considered in order to overcome potential resistance mechanism. An outbreak of NDM-1-producing *P. aeruginosa* in the ICU is particularly concerning and the only antimicrobial agent that exhibits in vitro activity against this pathogen would be cefiderocol. Once the pathogen and susceptibility results are available, antimicrobial treatment can be adjusted accordingly to maximize safety, efficacy, and cost-effectiveness.

