Xavier

78 yo; assisted living resident with indwelling urinary catheter; admitted to ICU with elevated fever and an altered mental state from baseline related to suspected cUTI

Physical findings and vital signs:

- Temperature: 102.8 °F
- Heart rate: 108 BPM
- Respiratory rate: 23 breaths/min
- Blood pressure: 104/68
- Suprapubic pain rated 9/10 by patient
- Heightened confusion from baseline and agitated mental state
- Severe flank pain
- Decreased urinary output

Medical history/concomitant conditions:

- Indwelling catheter
- Initiated on ceftazidime-avibactam in outpatient setting for UTI without improvement
- History of carbapenem-resistant *Escherichia coli* in urine cultures

Initial assessment:

- Symptoms suggestive of cUTI

Cultures:

- Presence of multidrug-resistant KPC-producing *Escherichia coli* with susceptibility to VABOMERE®
- KPC detected by immunochromotographic lateral flow assay

Performing AST as soon as possible can lead to improved clinical outcomes by ensuring patients with CRE receive early treatment with an appropriate antimicrobial therapy.[1,2]

This hypothetical case study is meant to be illustrative. It is not intended to offer medical advice. Determination of appropriate treatment is at the discretion of the physician.

Treatment results may vary by patient.

AST=antimicrobial susceptibility testing; CRE=carbapenem-resistant Enterobacterales; cUTI=complicated urinary infection; ICU=intensive care unit; KPC=*Klebsiella pneumoniae* carbapenemase; UTI=urinary tract infection.

START STRONG

VABOMERE®
meropenem and vaborbactam
for injection (4 g)

Early treatment with VABOMERE® (meropenem and vaborbactam) can benefit critically ill patients with cUTI caused by resistant, gram-negative pathogens[2,3]

Automated susceptibility testing finding:
Escherichia coli (99% probability)

Susceptibility information[4]

Antimicrobial	MIC (µg/mL)	Interpretation
Meropenem	≥4	Resistant
VABOMERE	≤4/8	Susceptible

Course of action and clinical outcome:

- First-line treatment with VABOMERE
- Resolution of signs and symptoms related to cUTI
- Clinical improvement after 4 days; discharged to assisted living facility to complete treatment with outpatient infusion services

This hypothetical case study is meant to be illustrative. It is not intended to offer medical advice. Determination of appropriate treatment is at the discretion of the physician.

Treatment results may vary by patient.

CLSI and FDA guidelines for meropenem, piperacillin/tazobactam, and VABOMERE are consistent.[4]

CLSI=Clinical and Laboratory Standards Institute; MIC=minimum inhibitory concentration.

INDICATIONS AND USAGE

VABOMERE® (meropenem and vaborbactam) is indicated for the treatment of patients 18 years of age and older with complicated urinary tract infections (cUTI) including pyelonephritis caused by the following susceptible microorganisms: *Escherichia coli*, *Klebsiella pneumoniae*, and *Enterobacter cloacae species* complex.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of VABOMERE® and other antibacterial drugs, VABOMERE® should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

DON'T WAIT TO TEST

Test for susceptibility to VABOMERE to provide early and effective treatment to your patients with cUTI caused by CRE.[1-3]

IMPORTANT SAFETY INFORMATION

Contraindications

VABOMERE® is contraindicated in patients with known hypersensitivity to any components of VABOMERE® (meropenem and vaborbactam), or to other drugs in the same class or in patients who have demonstrated anaphylactic reactions to beta-lactam antibacterial drugs.

Please see full Important Safety Information throughout and accompanying full Prescribing Information.

CRE risk and the benefits of early treatment

In the treatment of cUTI

VABOMERE®
meropenem and vaborbactam
for injection (4 g)

CRE presents a serious threat for critically ill patients

CRE infections are significantly more likely in patients with the following risk factors[5]:

- Chronic moderate-to-severe renal insufficiency[2,5,6]
- ≥3 comorbidities[5,6]
- Prior CRE infection[2,5]
- Immune compromise[2,5,7]
- Prolonged hospitalization or antibiotic therapy[2,5,7,8]
- Indwelling catheters[5-7]
- Long-term care in a nursing facility[2,7]

Benefits of early, appropriate therapy[9]

In an analysis of patients with CRE infections, those treated with an appropriate antibiotic within 48 hours of positive cultures (N=229) experienced improved clinical and economic outcomes compared with those who received delayed appropriate therapy (N=285).

3.5 fewer days of antibiotic therapy
(5.4 vs 8.9)

3.7 fewer days in the hospital
(5.1 vs 8.8)

14K
in-hospital savings
(11,539 vs 25,506)

100%
increase in likelihood of discharge home
(0.4 vs 0.2)

48%
decrease in likelihood of in-hospital death
(1.9 vs 3.7)

Retrospective database studies contain material limitations, and their results should be considered in light of the entire body of available evidence, including clinical trial data.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- Hypersensitivity reactions were reported in patients treated with VABOMERE® in the clinical trials. Serious and occasionally fatal hypersensitivity (anaphylactic) reactions and serious skin reactions have been reported in patients receiving therapy with beta-lactam antibacterial drugs. There have been reports of individuals with a history of penicillin hypersensitivity who have experienced severe hypersensitivity reactions when treated with another beta-lactam antibacterial drug. If an allergic reaction to VABOMERE® occurs, discontinue the drug immediately.

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VABOMERE efficacy and safety

In the treatment of cUTI

VABOMERE®
meropenem and vaborbactam
for injection (4 g)

Efficacy evaluated against a widely used cUTI treatment[3]

Clinical and microbiological response in the m-MITT population[3]

	VABOMERE % (n/N)	PIPERACILLIN/ TAZOBACTAM % (n/N)	DIFFERENCE (95% CI)
Overall success* (EOIVT)	98.4% (183/186)	94.3% (165/175)	4.1%† (0.3%, 8.8%)
Clinical cure plus eradication‡ (TOC)	76.5% (124/162)	73.2% (112/153)	3.3%§ (-6.2%, 13.0%)

*EOIVT includes patients with organisms resistant to piperacillin/tazobactam at baseline.[3]
†Primary endpoint: 4.1% treatment difference (95% CI, 0.3%, 8.8%) exceeded the lower limit for noninferiority and also superiority.[3,6]
‡TOC visit excludes patients with organisms resistant to piperacillin/tazobactam at baseline in both arms.[3]
§3.3% treatment difference (95% CI, -6.2%, 13%).[3]

Study description: A double-blind, double-dummy, randomized, multicenter noninferiority clinical trial evaluated 545 adult patients with cUTI, including acute pyelonephritis. Patients were treated with VABOMERE (meropenem 2 g and vaborbactam 2 g) or piperacillin/tazobactam (piperacillin 4 g/tazobactam 0.5 g) every 8 hours. After a minimum of 15 doses of IV therapy, patients who met prespecified criteria of improvement could be switched to oral levofloxacin.[3,6]

CI=confidence interval; EOIVT=end of intravenous treatment; IV=intravenous; m-MITT=microbiologically modified intention-to-treat; TOC=test of cure.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (cont'd)

- Seizures and other adverse Central Nervous System (CNS) experiences have been reported during treatment with meropenem, which is a component of VABOMERE®. Close adherence to the recommended dosage regimens is urged, especially in patients with known factors that predispose to convulsive activity.

Please see full Important Safety Information throughout and accompanying full Prescribing Information.

The majority of adverse events with VABOMERE were either mild or moderate in severity[6]

- There were fewer adverse reactions leading to discontinuations with patients receiving VABOMERE compared with patients receiving piperacillin/tazobactam (2.9% vs 5.1%)[3]
- The most frequently reported adverse reactions leading to discontinuation of VABOMERE were hypersensitivity (1.1%; n=3/272) and infusion-related reactions (0.7%; n=2/272)[3]

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (cont'd)

- Rhabdomyolysis has been reported with the use of meropenem, a component of VABOMERE®. If signs or symptoms of rhabdomyolysis such as muscle pain, tenderness or weakness, dark urine, or elevated creatine phosphokinase are observed, discontinue VABOMERE and initiate appropriate therapy.

2024 IDSA Guidance: The urgent public health risk of CRE in the US[10]

In the treatment of cUTI

VABOMERE®
meropenem and vaborbactam
for injection (4 g)

IDSA provides guidance on the treatment of antimicrobial-resistant infections. This 2024 update replaces previous versions of the guidance document.

See the full 2024 IDSA Guidance

Estimated

35%-48%

mortality rate for CRE infections[11,12]

35%-83%

of CRE cases are carbapenemase-producing isolates[13]

Patients who require devices (eg, catheters) and patients taking long courses of some antibiotics are most at risk for CRE infections[14]

CLSI=Clinical and Laboratory Standards Institute;
IDSA=Infectious Diseases Society of America.

IMPORTANT SAFETY INFORMATION

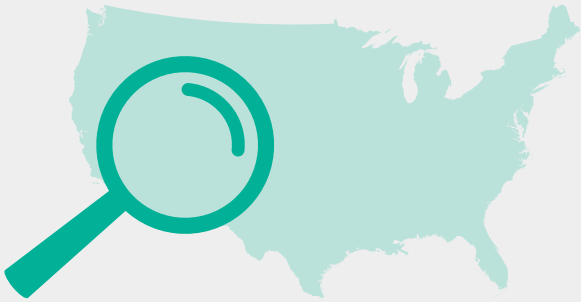
Warnings and Precautions (cont'd)

- *Clostridioides difficile*-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including VABOMERE®, and may range in severity from mild diarrhea to fatal colitis. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibacterial drug use not directed against *C. difficile* may need to be discontinued.

Carbapenemase testing and KPC prevalence

Both IDSA and CLSI strongly encourage all laboratories in the US to pursue carbapenemase testing to inform optimal treatment decisions.[13,15]

Of carbapenemase-producing CRE in the US,



80%-86% are KPC-producing strains, making KPC the most clinically relevant carbapenemase.[13]

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (cont'd)

- The concomitant use of VABOMERE® and valproic acid or divalproex sodium is generally not recommended. Case reports in the literature have shown that co-administration of carbapenems, including meropenem, to patients receiving valproic acid or divalproex sodium results in a reduction in valproic acid concentrations. The valproic acid concentrations may drop below the therapeutic range as a result of this interaction, therefore increasing the risk of breakthrough seizures. If administration of VABOMERE® is necessary, consider supplemental anticonvulsant therapy.

Please see full Important Safety Information throughout and accompanying full Prescribing Information.

2024 IDSA Guidance: Antimicrobial resistance[13]

In the treatment of cUTI
VABOMERE®
meropenem and vaborbactam
for injection (4 g)

Emergence of resistance to novel β-lactam antibiotics

While the emergence of resistance is a concern with all of the novel β-lactams used to treat CRE infections, IDSA notes that the frequency may be highest for ceftazidime-avibactam.

Estimated emergence of resistance after clinical exposure:

<5%
with VABOMERE

~10-20%
with ceftazidime-avibactam

IDSA recommends always repeating susceptibility testing for patients previously infected with CRE who present with symptoms suggestive of a new or relapsed infection.

Patients recently treated with ceftazidime-avibactam may be treated with a different novel β-lactam agent such as VABOMERE at least until culture and susceptibility data are available.

Development of clinical resistance in real-world use

In support of its findings, the IDSA discusses a single observational study comparing the clinical outcomes of 26 patients who received VABOMERE and 105 patients who received ceftazidime-avibactam for at least 72 hours for the treatment of CRE infections.

Percentage of patients with recurrent CRE infections who developed resistance to initial therapy:

0%
with VABOMERE (n=0/3)

20%
with ceftazidime-avibactam (n=3/15)

Observational studies contain material limitations, and their results should be considered in light of the entire body of available evidence, including clinical trial data.

The statements on these pages are not intended to imply comparable safety or effectiveness between VABOMERE® (meropenem and vaborbactam) and ceftazidime-avibactam. Consult the respective products' Prescribing Information for further details, including complete indication and Important Safety Information.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (cont'd)

- In patients with renal impairment, thrombocytopenia has been observed in patients treated with meropenem, but no clinical bleeding has been reported.
- Alert patients receiving VABOMERE® on an outpatient basis regarding adverse reactions such as seizures, delirium, headaches and/or paresthesias that could interfere with mental alertness and/or cause motor impairment.

Please see full Important Safety Information throughout and accompanying full Prescribing Information.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (cont'd)

- Prescribing VABOMERE® in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of drug-resistant bacteria.
- As with other antibacterial drugs, prolonged use of VABOMERE® may result in overgrowth of nonsusceptible organisms.

The benefits of infusion services settings

In the treatment of cUTI

VABOMERE®
meropenem and vaborbactam
for injection (4 g)

14% **of VABOMERE doses were administered in outpatient infusion services settings in 2024[16]**

Infusion services for gram-negative infections are increasingly prevalent, providing patients with the following benefits:

Avoiding hospital-acquired infections
Prevent exposure to other patients with transmittable diseases[17]

Increasing patient satisfaction
Treatment in home settings, including through the **use of elastomeric pumps,** may offer **greater flexibility of care**[17,18]

Optimizing treatment accessibility
Increase flexibility and empower patients with a solution in the comfort of their own home or outpatient infusion center[17,19,20]

Reducing healthcare burden
Shorten inpatient stays and reduce readmissions through seamless transitions of care[19,21,22]

After in-hospital initiation, stable patients with cUTI and CRE risk factors are appropriate for outpatient infusion services.

IMPORTANT SAFETY INFORMATION

Adverse Reactions

The most frequently reported adverse reactions occurring in ≥3% of patients treated with VABOMERE® were headache, phlebitis/infusion site reactions, and diarrhea.

Please see full Important Safety Information throughout and accompanying full Prescribing Information.

IMPORTANT SAFETY INFORMATION

Contraindications

VABOMERE® is contraindicated in patients with known hypersensitivity to any components of VABOMERE® (meropenem and vaborbactam), or to other drugs in the same class or in patients who have demonstrated anaphylactic reactions to beta-lactam antibacterial drugs.

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IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- Hypersensitivity reactions were reported in patients treated with VABOMERE® in the clinical trials. Serious and occasionally fatal hypersensitivity (anaphylactic) reactions and serious skin reactions have been reported in patients receiving therapy with beta-lactam antibacterial drugs. There have been reports of individuals with a history of penicillin hypersensitivity who have experienced severe hypersensitivity reactions when treated with another beta-lactam antibacterial drug. If an allergic reaction to VABOMERE® occurs, discontinue the drug immediately.

Please see full Important Safety Information throughout and accompanying full Prescribing Information.

CRE poses an urgent threat[2,5-8,10]

- Critically ill patients are at greater risk of being infected and experiencing poor outcomes

Early testing and treatment are essential[1,2]

- Early treatment of CRE cUTI is associated with improved outcomes, and susceptibility testing is essential to providing effective treatment sooner

Infusion services provide flexibility for appropriate patients[17-22]

- Increase patient satisfaction and reduce healthcare burden with flexible infusion care

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (cont'd)

- Seizures and other adverse Central Nervous System (CNS) experiences have been reported during treatment with meropenem, which is a component of VABOMERE®. Close adherence to the recommended dosage regimens is urged, especially in patients with known factors that predispose to convulsive activity.

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melinta therapeutics

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PP-VAB-US-0554