2024 IDSA UPDATE

Guidance from the Infectious Diseases Society of America (IDSA) recommends VABOMERE®

VABOMERE®
meropenem and vaborbactam
for injection (4 g)

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

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.

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

The urgent public health risk of CRE in the US[1]

Estimated

35%-48%

mortality rate for CRE infections[2,3]

up to 83%

of CRE cases are carbapenemase-producing isolates[4]

Patients who require devices (eg, catheters) and patients taking long courses of some antibiotics are most at risk for CRE infections[5]

Of carbapenemase-producing CRE in the US, **80%-86% are KPC-producing strains, making KPC the most clinically relevant carbapenemase.**[4]

CRE=carbapenem-resistant Enterobacterales; KPC=Klebsiella pneumoniae carbapenemase.

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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VABOMERE® for CRE cUTI[6]

Specifically designed for KPC-producing CRE

- VABOMERE® (meropenem and vaborbactam) combines meropenem, a trusted carbapenem, with vaborbactam, a unique β-lactamase inhibitor

Addresses a broad spectrum of gram-negative pathogens

- VABOMERE has demonstrated clinical activity against most *E coli*, *K pneumoniae*, and *E cloacae species* complex isolates
- VABOMERE has demonstrated in vitro activity against Enterobacterales that produce β-lactamases and extended-spectrum β-lactamases (ESBLs): KPC, SME, TEM, SHV, CTX-M, CMY, and ACT*

*In vitro activity does not necessarily correlate with clinical efficacy.

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.

Approaches to empiric therapy[4]

Empiric treatment decisions should be guided by:

- Most likely pathogen
- Most likely source of infection
- Severity of illness
- Any additional patient-specific factors, including severe penicillin allergy and chronic kidney disease

IDSA Guidance recommends treatment decisions be refined based on[4]:

- The identity and AST profile of the pathogen
- Any prominent β-lactamase genes that have been identified

AST=antimicrobial susceptibility testing.

Carbapenemase testing[4]

Carbapenemase testing is important in guiding treatment decisions, as newer β-lactam antibiotics have activity against specific carbapenemases.

Phenotypic tests differentiate carbapenemase and non-carbapenemase-producing CRE.

Genotypic tests identify the specific carbapenemase produced by the CRE isolate.

Clinical microbiology laboratories are strongly encouraged to implement genotypic tests.[4]

IDSA recommendations for the use of VABOMERE®[4]

VABOMERE® (meropenem and vaborbactam) is a preferred treatment option for cUTI or pyelonephritis caused by CRE

VABOMERE is also a preferred treatment option for infections caused by CRE that are not carbapenemase producing and that do not exhibit susceptibility to any carbapenem

IDSA recommendations assume that in vitro activity of antibiotics is demonstrated.[4]

Recommendations from 2024 IDSA Guidance, CRE section, Questions 3.2 and 3.3.

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 within and accompanying full Prescribing Information.

VABOMERE is slightly favored for KPC-producing infections followed by ceftazidime-avibactam and imipenem-cilastatin-relebactam

- Guidance is based on available data regarding clinical outcomes and emergence of resistance
  - Clinical cure and 30-day mortality rates between patients who received VABOMERE and patients who received ceftazidime-avibactam numerically favored VABOMERE in an observational study
- IDSA suggests reserving cefiderocol for the treatment of infections caused by metallo-β-lactamase-producing Enterobacterales or glucose non-fermenting gram-negative organisms

Recommendations from 2024 IDSA Guidance, CRE section, Question 3.4.

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.

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Emergence of resistance to novel β-lactam antibiotics[4]

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

These statements 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.

IDSA recommends repeating susceptibility testing for patients previously infected with CRE who present with symptoms suggestive of a new or relapsed infection.[4]

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.[4]

Development of clinical resistance in real-world use[4]

In support of its findings, IDSA discussed 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)

These statements are not intended to imply comparable safety or effectiveness between VABOMERE and ceftazidime-avibactam. Consult the respective products' Prescribing Information for further details, including complete indication and Important Safety Information. Observational 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 (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.

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

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (cont'd)

- As with other antibacterial drugs, prolonged use of VABOMERE may result in overgrowth of nonsusceptible organisms.

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Overview of IDSA recommendations for the use of VABOMERE®[4]

- **VABOMERE® (meropenem and vaborbactam) is a preferred treatment option for cUTI or pyelonephritis caused by CRE**
- **VABOMERE is also a preferred treatment option for infections caused by CRE that are not carbapenemase producing and that do not exhibit susceptibility to any carbapenem**
- **VABOMERE is slightly favored for KPC-producing infections followed by ceftazidime-avibactam and imipenem-cilastatin-relebactam**

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 accompanying full Prescribing Information.

References: 1. Tadese BK, Darkoh C, DeSantis SM, Mgbere O, Fujimoto K. *J Glob Antimicrob Resist*. 2022;30:222-227. doi:10.1016/j.jgar.2022.06.019 **2.** Patel G, Huprikar S, Factor SH, Jenkins SG, Calfee DP. *Infect Control Hosp Epidemiol*. 2008;29(12):1099-1106. doi:10.1086/592412 **3.** de Maio Carrilho CMD, de Oliveira LM, Gaudereto J, et al. *BMC Infect Dis*. 2016;16(1):629. doi:10.1186/s12879-016-1979-z **4.** Tamma PD, Heil EL, Justo JA, et al. Infectious Diseases Society of America 2024 guidance on the treatment of antimicrobial resistant gram-negative infections. Infectious Diseases Society of America. Accessed December 31, 2023. https://www.idsociety.org/practice-guideline/amr-guidance/ **5.** Antibiotic resistance threats in the United States, 2019. Centers for Disease Control and Prevention. Accessed August 26, 2024. https://www.cdc.gov/antimicrobial-resistance/data-research/threats/index.html **6.** VABOMERE [package insert]: Melinta Therapeutics, LLC.

melinta therapeutics

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