# MDR Gram-Negative Management Protocal

**1** Patient is admitted to the Intensive Care Unit (ICU) after his fever spikes and his vitals rapidly decline.

**2** The critical care physician examines the patient and takes a detailed history. Based on the symptoms and history including the unit in the hospital that sent the patient to the ICU, the physician believes that the patient has a serious infection. The critical care physician immediately takes a specimen and sends it to the microbiology lab to be cultured. Empiric antibiotic therapy is ordered based on the hospital's AMS guidelines for the suspected source of infection. The critical care physician may adjust dose and duration based on any complicating risk factors found in the patient history. Note: The critical care physician must follow the protocol and use an antibiotic on formulary. ID Consult is needed to order any antibiotic not on formulary or in a protocol.

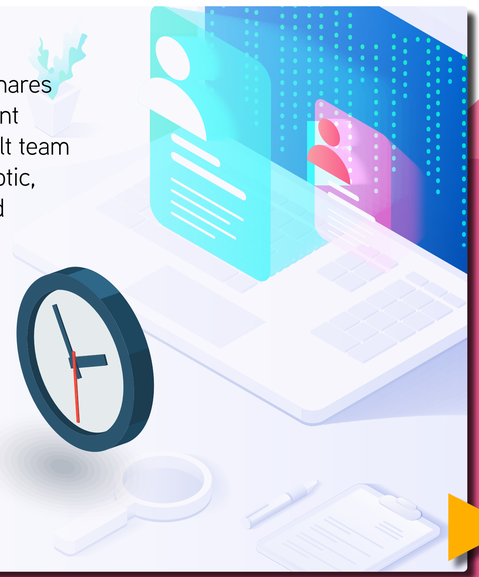
**RISK FACTORS:**

- Gender
- Age
- Ethnicity
- Previous UTI
- Previous Antibiotics
- Previous Hospitalization
- Recent Travel
- Nursing Home Resident
- Diabetes
- Immunocompromised
- Catheterization

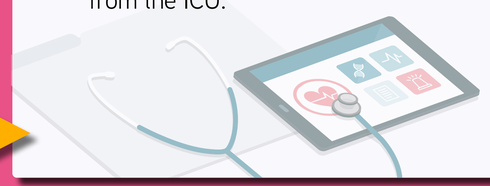
**3** The microbiology lab receives the lab request from the critical care physician and tests to identify the pathogen and determine susceptibility against a standard list of antibiotics. If the results show a MDR Gram-negative pathogen, the lab runs an additional MDR panel which will include antibiotics (typically newer agents) that may have susceptibility to the known pathogen. The microbiologist informs the ID PharmD and ID Physician that an MDR Gram-negative pathogen was identified which triggers an ID Consult.

**4** The ID PharmD and the ID Physician review and interpret the microbiology results. Together they consult with the Critical Care physician to adjust the antibiotic therapy.

**5** The critical care physician shares the patient history and current status to assist the ID Consult team in identifying the right antibiotic, right dose, right duration and right route. The team considers the patient's comorbidities and possible drug-drug interactions. Time is critical because the patient has not improved. An alternative antibiotic is ordered.



**6** The antibiotic is switched and the patient responds well. The critical care physician continues to monitor the patient. Their goal is to stabilize the patient and ultimately discharge from the ICU.



**7** The ID physician and ID pharmacist, round in the ICU to monitor the patient's progress and record any adverse events. Dose adjustments are made as needed following de-escalation protocols.

**8** After a few days the patient is stable and discharged from the ICU and heads back to the medical floor to complete their recovery.



SUPERION PHARMACEUTICALS

# Review of VABOMERE®

*(meropenem and vaborbactam) for injection, for intravenous use*


from Melinta THERAPEUTICS

*Not actual product. For illustrative purposes only. See Vabomere PI for full prescribing information.*

## Indications and Usage[1]

**Complicated Urinary Tract Infections (cUTI), including Pyelonephritis**

- VABOMERE® 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.

## Microbiology[1]

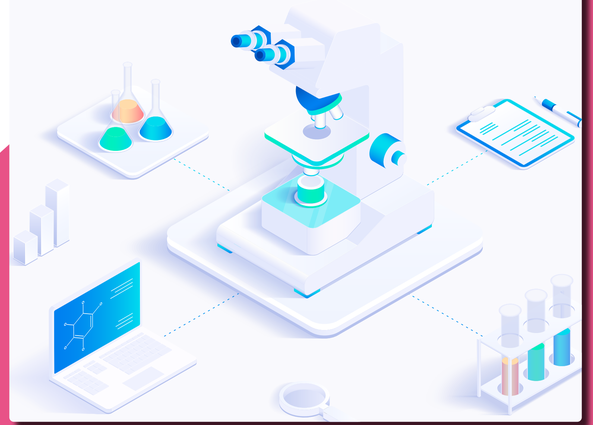
The following *in vitro* data are available, but their clinical significance is unknown. At least 90 percent of the following bacteria exhibit an *in vitro* MIC less than or equal to the susceptible breakpoint for VABOMERE:

- Gram-negative bacteria:
  - *Citrobacter freundii*
  - *Citrobacter koseri*
  - *Enterobacter aerogenes*
  - *Klebsiella oxytoca*
  - *Morganella morganii*
  - *Proteus mirabilis*
  - *Providencia spp.*
  - *Pseudomonas aeruginosa*
  - *Serratia marcescens*

**Resistance Mechanisms**

VABOMERE may not have activity against Gram-negative bacteria that have porin mutations combined with overexpression of efflux pumps.

VABOMERE demonstrated *in vitro* activity against Enterobacteriaceae in the presence of some beta-lactamases and extended-spectrum beta-lactamases (ESBLs) of the following groups: KPC, SME, TEM, SHV, CTX-M, CMY, and ACT. VABOMERE is not active against bacteria that produce metallo-beta lactamases or oxacillinases with carbapenemase activity.

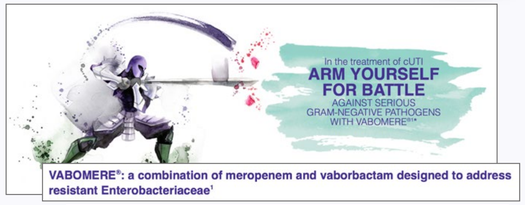


## Dosage/Administration[1]

- 4 grams administered every 8 hours by intravenous (IV) infusion over 3 hours in patients ≥18 years of age with estimated glomerular filtration rate (eGFR) ≥50 mL/min/1.73 $m^2$
- 4 g of VABOMERE = 2 g meropenem and 2 g of vaborbactam
- Dosage adjustment is recommended in patients with renal impairment who have an eGFR <50 mL/min/1.73 $m^2$
- The duration of treatment is for up to 14 days

## Other/Marketing Messages[3]

Marketed by Melinta Therapeutics




## Susceptibility Testing[3]

**Automated testing:**

- Beckman Coulter: MicroScan® MIC Panels
- Becton Dickinson: BD Phoenix™ Emerge™ Gram-negative susceptibility panels

**Manual and semi-automated testing:**

- bioMérieux: ETEST®
- Liofilchem®: MIC Test Strip
- Hardy Diagnostics™: Susceptibility Disk
- Thermo Fisher Scientific: Thermo Scientific™ Oxoid Disk and Sensititre™ MIC plated

## Clinical Data[1]

A total of 545 adults with cUTI, including pyelonephritis were randomized into a double-blind, double dummy, multi-center trial comparing VABOMERE (meropenem 2 grams and vaborbactam 2 grams) to piperacillin/tazobactam (piperacillin 4 grams/tazobactam 0.5 grams) intravenously every 8 hours. Switch to an oral antibacterial drug, such as levofloxacin was allowed after a minimum of 15 doses of IV therapy.

**Clinical and Microbiological Response Rates in a Phase 3 Trial of cUTI Including Pyelonephritis (m-MITT Population)**

| | VABOMERE n/N (%) | Piperacillin/ Tazobactam n/N (%) | Difference (95% CI) |
|---|---|---|---|
| **Clinical cure or improvement AND microbiological eradication at the End of IV Treatment Visit*** | 183/186 (98.4) | 165/175 (94.3) | 4.1% (0.3%, 8.8%) |
| **Clinical cure AND microbiological eradication at the Test of Cure visit approximately 7 days after completion of treatment**** | 124/162 (76.5) | 112/153 (73.2) | 3.3% (-6.2%, 13.0%) |

CI = confidence interval; EOIVT = End of Intravenous Treatment; TOC = Test of Cure
*End of IV Treatment visit includes patients with organisms resistant to piperacillin/tazobactam at baseline
**Test of Cure visit excludes patients with organisms resistant to piperacillin/tazobactam at baseline

## Adverse Reactions[1]

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

## Price[2]

WAC/Vial $178

WAC/Day $1,069



1 Vabomere (prescribing information), February 2019, Lincolnshire, IL, Melinta Therapeutics, Inc.
2 Data on file, Shionogi & Co., Ltd. Osaka, Japan March 2020
3 Melinta Therapeutics, Inc. Vabomere website: https://www.vabomere.com Accessed March 9, 2020

SUPERION PHARMACEUTICALS