ICD-10-PCS Request

VABOMERE™
(meropenem-vaborbactam for injection)

September 2018 ICD-10 Coordination
and Maintenance Committee Meeting

Overview: New ICD-10-PCS Code Is Needed for Administration of Vabomere™

Issue: There is currently no unique ICD-10-PCS code to describe the administration of Vabomere™ (meropenem-vaborbactam).

New Technology Application? Yes, a New Technology Add-on Payment (NTAP) application was submitted and was approved for Vabomere™ (meropenem-vaborbactam) for FY 2019.

Food & Drug Administration (FDA) Approved? Yes, Vabomere™ received FDA approval on August 29, 2017; Vabomere™ also received Qualified Infectious Disease Product (QIDP) status from FDA.

- Vabomere™ was developed to address certain gram-negative bacteria, widely considered to be one of the largest current areas of unmet medical need, as these pathogens are growing increasingly resistant to existing therapies with few antibiotics in development.
- Vabomere™ is FDA-approved 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 (E. coli)*, *Klebsiella pnemoniae*, and *Enterobacter cloacae species* complex.
- As reflected in the FDA-approved labeling, Vabomere™ in vitro data also show susceptibility for the following gram-negative bacteria: *Citrobacter freundii, Citrobacter koseri, Enterobacter aerogenes, Klebsiella oxytoca, Morganella morganii, Proteus mirabilis, Providencia spp., Pseudomonas aeruginosa, Serratia marcescens.*
- Vabomere™ has been shown, as noted in the FDA-approved labeling, to be active against a number of different gram-negative bacteria, including carbapenem-resistant Enterobacteriaceae (CRE).
- See Vabomere™ Prescribing Information (PI) Sections 1.1, 1.2, 12.4.

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Carbapenem-resistant Enterobacteriaceae (CRE): A Clear, Present, and Mounting Unmet Need

Vabomere™ was developed specifically in response to the urgent and growing threat of CRE.

Global and national reports have focused on the urgent threat posed by CRE in particular. For example:

- **CDC Antibiotic Resistance Threats Report (2013)[1]**
  - More than 2 million people are infected with bacteria that are resistant to antibiotics annually
  - At least 23,000 people die each year as a direct result of these antibiotic-resistant infections
  - Urgent threat: Carbapenem-resistant Enterobacteriaceae (CRE)
- **Tackling Drug-resistant Infections Globally: Final Report and Recommendations (May 2016)[2]**
  - Annual deaths globally due to antimicrobial resistance pathogens are expected to exceed th sum contribution from cancer and diabetes by 2050
  - This death rate could cost the world up to 100 trillion USD; each person in the world today will be more than 10,000 USD worse off
- **WHO priority pathogens list for R&D of new antibiotics (Feb 2017)[3]**
  - CRITICAL PRIORITY: *Enterobacteriaceae*, carbapenem-resistant, 3rd generation cephalosporin resistant
- **White House Counsel on Combating Antibiotic Resistant Bacteria Draft Report (Sep. 2017)[4]**
  - "[T]he existence and availability of a diverse array of antibiotics acts as insurance against future epidemics"; "this availability should be considered as a metric when the USG, other governments, payers, and other potential investors consider the value of these drugs."

Review on Antimicrobial Resistance

Tackling drug-resistant infections globally

World Health Organization

1. Centers for Disease Control and Prevention. Antibiotic Resistance Threats in the United States, 2013. Atlanta: CDC; 2013.
2. Tackling Drug-Resistant Infections Globally: Final Report and Recommendations. UK, 2016. HM Government and Wellcome Trust.
3. World Health Organization. Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. February 27, 2017.
4. White House Counsel on Combating Antibiotic Resistant Bacteria. Recommendations for Incentivizing the Development of Therapeutics Diagnostics and Vaccines to Combat Antibiotic Resistance

Vabomere™: Description and Method of Action

- Description and Method of Action. Vabomere™ uses the first-in-class beta lactamase inhibitor vaborbactam to treat new patient populations by causing carbapenem-resistant infections to be sensitive to meropenem.
  - The **vaborbactam** component of Vabomere™ is a non-suicidal beta-lactamase inhibitor that protects meropenem from degradation by certain serine beta-lactamases such as *Klebsiella pneumoniae* carbapenemase (KPC).
    - Vaborbactam, while it alone does not have any antibacterial activity, it allows for the treatment of resistant infections by disarming the resistant properties of the bacteria so that they are sensitive to meropenem.
    - Vaborbactam does not decrease the activity of meropenem against meropenem-sensitive organisms, but it facilitates and is essential to the novel approach to fighting resistant infections by causing resistant infections to be sensitive to meropenem
  - The **meropenem** component of Vabomere™ is a penem antibacterial drug.
    - The bactericidal action of meropenem results from the inhibition of cell wall synthesis.
    - Meropenem penetrates the cell wall of most gram-positive and gram-negative bacteria to bind penicillin-binding protein (PBP) targets.

Vabomere™ protects meropenem from degradation by certain CRE strains producing the KPC enzyme, thereby providing a therapeutic effect where bacteria would otherwise be resistant and unresponsive to treatment.

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Vabomere™ Clinical Data: Brief Overview

- With respect to clinical trial data, at a very high level:
  - The pivotal clinical trial found that Vabomere™ is a safe and effective new FDA-approved treatment option for cUTI including acute pyelonephritis, including in renally impaired patients when the dose is adjusted as recommended in the U.S. Prescribing Information.
  - In a non-pivotal, pathogen based clinical trial, Vabomere™ was associated with decreased mortality, increased clinical cure, and reduced nephrotoxicity compared with BAT in the treatment of CRE infections.
- Additional in vitro data also have shown the activity of Vabomere™ against CRE-producing bacteria, including CRE-producing strains of the KPC enzyme.
  - The KPC enzyme is known to produce CRE, and KPC results in resistance to carbapenems. (See reports discussed and cited on Slide 3 of this presentation.)
- The FDA-approved labeling (see PI sections 1.1, 1.2, 12.4) discusses Vabomere™'s activity against bacteria that produce beta-lactamases, including KPC.
- Accordingly, Vabomere™ is a new antibiotic that has demonstrated activity against KPC-producing CRE and that is approved by FDA to treat cUTI including pyelonephritis caused by these specific and potentially highly resistant bacteria.

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Vabomere™: Inpatient Administration

- Inpatient Administration of Vabomere™.
  - The recommended dosage of Vabomere™ is 4 grams (meropenem 2 grams and vaborbactam 2 grams) administered every 8 hours by intravenous (IV) infusion over 3 hours in patients 18 years of age and older with an estimated glomerular filtration rate (eGFR) greater than or equal to 50 mL/min/1.73m2.
  - The duration of treatment is for up to 14 days.
  - Per the FDA-approved labeling, dosage adjustment is recommended in patients with renal impairment who have an eGFR less than 50 mL/min/1.73m2.
  - See Vabomere™ Full Prescribing Information, available at http://www.vabomere.com/media/pdf/vabomere-us-prescribing-information.pdf, for additional information and details.

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Thank You!