APPLICATION NUMBER:

209776Orig1s000

RISK ASSESSMENT and RISK MITIGATION REVIEW(S)
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<tr>
<th>Application Type</th>
<th>NDA</th>
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<tr>
<td>Application Number</td>
<td>209776</td>
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<td>PDUFA Goal Date</td>
<td>August 29, 2017</td>
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<tr>
<td>OSE RCM #</td>
<td>2017-7; 2017-9</td>
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<tr>
<td>Reviewer Name(s)</td>
<td>Till Olickal, Ph.D., Pharm.D.</td>
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<td>OMEPRM Review Completion Date</td>
<td>June 27, 2017</td>
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<tr>
<td>Subject</td>
<td>Review to determine if a REMS is necessary</td>
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<tr>
<td>Established Name</td>
<td>Meropenem-Vaborbactam</td>
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<tr>
<td>Trade Name</td>
<td>Vabomere</td>
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<tr>
<td>Name of Applicant</td>
<td>Rempex Pharmaceuticals</td>
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<tr>
<td>Therapeutic Class</td>
<td>Combination product consisting of meropenem, a carbapenem-class antibacterial agent, and vaborbactam, a beta-lactamase inhibitor.</td>
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<tr>
<td>Formulation(s)</td>
<td>Injection is supplied as a sterile powder for constitution in single-use vials containing meropenem 1 g and vaborbactam 1 g.</td>
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<tr>
<td>Dosing Regimen</td>
<td>4 grams (meropenem 2 g and vaborbactam 2 g) administered every 8 hours by intravenous (IV) infusion over 3 hours.</td>
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EXECUTIVE SUMMARY

This review by the Division of Risk Management (DRISK) evaluates whether a risk evaluation and mitigation strategy (REMS) for the new molecular entity meropenem-vaborbactam is necessary to ensure the benefits outweigh its risks. Rempex Pharmaceuticals submitted a New Drug Application (NDA) 209776 for meropenem-vaborbactam with the proposed indication for the treatment of complicated urinary tract infections, including pyelonephritis. The risks associated with meropenem-vaborbactam are hypersensitivity, seizures and Clostridium difficile-associated diarrhea. The applicant did not submit a REMS with this application but proposed Prescribing Information that includes Warnings and Precautions.

DRISK and DAIP have determined that if approved, a REMS is not necessary to ensure the benefits of meropenem/vaborbactam outweigh its risks. Meropenem-vaborbactam could provide an alternative treatment option as broad spectrum coverage for the treatment of complicated urinary tract infection (cUTI)/pyelonephritis, especially to address resistance in gram-negative bacteria due to Klebsiella pneumoniae carbapenemase (KPC)-producing carbapenem-resistant Enterobacteriaceae (CRE). In the clinical trial, meropenem/vaborbactam appeared efficacious in both its primary and secondary outcomes. Meropenem/vaborbactam demonstrated an overall favorable safety profile for the treatment of cUTI/pyelonephritis. Although no significant safety signals were detected in this review, the meropenem/vaborbactam prescribing information will include safety information contained in the current meropenem label, in Warnings and Precautions. The most concerning adverse reactions associated with the use of meropenem/vaborbactam are hypersensitivity, seizures and Clostridium difficile-associated diarrhea; these risks will be communicated in the Warnings and Precautions section of the product label.

1 Introduction

This review by the Division of Risk Management (DRISK) evaluates whether a risk evaluation and mitigation strategy (REMS) for the new molecular entity (NME) meropenem-vaborbactam is necessary to ensure the benefits outweigh its risks. Rempex Pharmaceuticals submitted a New Drug Application (NDA) 209776 for meropenem-vaborbactam with the proposed indication for the treatment of complicated urinary tract infections, including pyelonephritis. This application is under review in the Division of Anti-Infective Products (DAIP). The applicant did not submit a REMS with this application but proposed Prescribing Information that includes warnings and precautions to address the risks of hypersensitivity, seizures and Clostridium difficile-associated diarrhea.

2 Background

2.1 PRODUCT INFORMATION

Meropenem-vaborbactam, a NME, is a combination product consisting of meropenem, a carbapenem-class antibacterial agent, and vaborbactam, a beta-lactamase inhibitor; proposed for indication as treatment of complicated urinary tract infections, including pyelonephritis. The bactericidal action of meropenem results from the inhibition of cell wall synthesis. The vaborbactam component is a non-beta-lactam non-suicidal inhibitor of certain serine beta-lactamases with a particular potent activity against Klebsiella pneumoniae carbapenemase (KPC). By inhibiting KPC and related beta-lactamases, vaborbactam protects meropenem from degradation by these enzymes. Meropenem-vaborbactam is
supplied as a sterile powder for reconstitution in single-use vials containing meropenem 1 g and vaborbactam 1 g for intravenous (IV) injection. For the treatment of patients 18 years and older with complicated urinary tract infections, including pyelonephritis, the proposed regimen of meropenem-vaborbactam is 4 grams (meropenem 2 g and vaborbactam 2 g) administered every 8 hours by intravenous (IV) infusion over 3 hours. The duration of treatment is for up to 14 days. Meropenem-vaborbactam was granted a Qualified Infectious Disease Products (QIDP) designation on December 19, 2013, and a fast track designation on March 21, 2016. Meropenem-vaborbactam is a new molecular entity (NME) NDA type 505(b)(2) pathway application. Meropenem-vaborbactam is not currently approved in any jurisdiction.

2.2 REGULATORY HISTORY

The following is a summary of the regulatory history for meropenem-vaborbactam (NDA 209776) relevant to this review:

- 12/19/2013: Qualified Infectious Disease Products (QIDP) designation request for meropenem/RPX7009 was granted for the indications of complicated urinary tract infections, complicated intra-abdominal infections, hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia, catheter-related bloodstream infections, febrile neutropenia.
- 12/24/2013: Investigation New Drug (IND) 120040 submission was received.
- 03/21/2016: Fast track designation granted
- 11/03/2016: Applicant informed at pre-NDA meeting that the need for a REMS for meropenem-vaborbactam will be made upon reviewing the NDA. With regard to the Medication Guide, given that meropenem-vaborbactam will be administered intravenously and mainly in the inpatient setting, a Medication Guide may not be needed. Applicant was also informed that a final decision can only be made upon the review of the NDA.
- 12/29/2016: NDA 209776 submission for meropenem-vaborbactam with the proposed indication for the treatment of complicated urinary tract infections, including pyelonephritis, received.
- 04/12/2017: A Post Mid-cycle meeting was held between the Agency and the Applicant via teleconference. The Agency informed the Applicant that based on the currently available data, there were no safety issues that require a REMS for meropenem-vaborbactam.

3 Therapeutic Context and Treatment Options

3.1 DESCRIPTION OF THE MEDICAL CONDITION

Urinary tract infection (UTI) is a significant health problem in both community and hospital-based settings. It is estimated that 150 million UTIs occur yearly worldwide, accounting for $6 billion in healthcare expenditures. The majority of community-acquired UTIs manifest as uncomplicated bacterial cystitis, and occur mainly in females. In the health-care setting, approximately 40% of all nosocomial

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*a* Section 505-1 (a) of the FD&C Act: **FDAAA factor (D): The expected or actual duration of treatment with the drug.**

*b* Section 505-1 (a) of the FD&C Act: **FDAAA factor (F): Whether the drug is a new molecular entity.**
infections are UTIs, and most are associated with the use of urinary catheters. Uncomplicated UTI is an infection in a healthy patient with anatomically and functionally normal urinary tract. Complicated UTI is an infection associated with factors increasing colonization and decreasing efficacy of therapy. This requires one or all of following: anatomic or functional abnormality of urinary tract (enlarged prostate, stone disease, diverticulum, neurogenic bladder, etc.), immunocompromised host, and multi-drug resistant bacteria. The urinary tract is a common source of life-threatening infections, and an important cause of sepsis in patients admitted to hospital wards, emergency departments, and intensive care units. Urosepsis is associated with mortality of 20–40% in critically ill patients. Treatment of complicated urinary-tract infections, which can affect the lower urinary tract or upper urinary tract (pyelonephritis), is becoming increasingly challenging because of extending antimicrobial resistance; most uropathogens implicated in health-care-associated complicated urinary-tract infections, including catheter related infections, are resistant to multiple antimicrobial agents.

3.2 DESCRIPTION OF CURRENT TREATMENT OPTIONS

Worldwide, fluoroquinolones are the most frequently used antibacterials for the treatment of complicated urinary-tract infections (26.7%), followed by cephalosporins (23.3%), aminoglycosides (14.1%), and penicillins (13.8%), despite global resistance rates being 35–50% for these antibiotics. Importantly, inappropriate or inadequate treatment of these common infections can result in poor clinical outcomes and place substantial burden on the health-care system. Beta-lactam antibiotics are among the most useful classes of antibiotics to treat gram-negative infections. The growth in resistance to beta-lactam antibiotics, including the carbapenems, among relatively common bacteria has been the “tipping point” for gram-negative infections becoming untreatable by modern antimicrobials agents. Thus, the United States (US) Centers for Disease Control and Prevention (CDC) considers resistance by several gram-negative pathogens to beta-lactam antibiotics as a serious or urgent antimicrobial resistance threat; in particular, the dissemination of the *Klebsiella pneumoniae* carbapenemase (KPC) and subsequent spread of carbapenem-resistant Enterobacteriaceae (CRE) is a global concern. CRE, *Clostridium difficile*, and drug-resistant *Neisseria gonorrhoeae* are the three urgent antimicrobial resistance threats identified by CDC along with, with CRE being the only pathogen of the three that causes systemic infections at multiple body sites. An estimated 140,000 healthcare-associated Enterobacteriaceae infections occur in the United States each year; about 9,300 of these are caused by CRE.

Meropenem is a broad-spectrum (gram-positive, gram-negative, and anaerobic bacteria), injectable, carbapenem antibiotic that has been used worldwide for over 2 decades for the treatment of serious infections. Meropenem is considered to be efficacious, safe, and well tolerated. Recent nonclinical and clinical studies have demonstrated that meropenem doses of 2 g every 8 hours administered as a prolonged infusion provides optimized PK-PD exposures that are associated with improved bacterial killing and clinical response. Vaborbactam is the first beta-lactamase inhibitor in a novel chemical class, cyclic boronates, for potent inhibition of Class A serine carbapenemases, specifically the KPC enzyme.

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^c Section 505-1 (a) of the FD&C Act: FDAAA factor (A): The estimated size of the population likely to use the drug involved.

d Section 505-1 (a) of the FD&C Act: FDAAA factor (B): The seriousness of the disease or condition that is to be treated with the drug.
Meropenem-vaborbactam is a combination product designed to address resistance in gram-negative bacteria, in particular due to KPC-producing CRE.7

4 Benefit Assessment

The pivotal trial (study 505) supporting this application was a randomized, multi-center, double blind, double-dummy noninferiority trial to evaluate the efficacy, safety, and tolerability of meropenem 2 g-vaborbactam 2 g compared with piperacillin/tazobactam in the treatment of adults with complicated urinary tract infections (cUTI) or acute pyelonephritis (AP). A total of 545 adults were randomized in a 1:1 ratio to receive either meropenem/vaborbactam (n=272) or piperacillin/tazobactam (n=273), considered as MIIT (modified intent-to-treat) population. The MITT population, a subset of the ITT population, received at least one dose of study drug. The MITT population is the same population that was used for the safety analysis. The m-MITT (microbiologic evaluable modified-ITT) is the subset of the MITT population and is the population in which the primary outcome was evaluated from a total of 374 patients randomized to receive either meropenem/vaborbactam (n=192) or piperacillin/tazobactam (n=182). Patients in the meropenem/vaborbactam group received meropenem 2 g-vaborbactam 2 g diluted in normal saline to a volume of 250 mL and infused over 3 hours and to preserve the blind, 100 mL normal saline infused over 30 minutes q8h. Patients in the piperacillin/tazobactam group received piperacillin/tazobactam 4.5 g (piperacillin 4 g /tazobactam 0.5 g) diluted in normal saline to a volume of 100 mL and infused over 30 minutes and to preserve the blind, 250 mL normal saline infused over 3 hours q8hr. Patients could switch to oral therapy after minimum of 15 doses of IV study drug if they met all step-down criteria for switching to oral therapy. Total treatment duration (intravenous plus/minus oral) was 10 days of therapy or up to 14 days in patients with baseline bacteremia.

The primary efficacy endpoint in this trial was defined as Overall Response at the end of IV treatment (EOIVT) visit in the m-MITT population, which was defined as the randomized patients who received at least one dose of study drug and had a baseline bacterial pathogen(s) of >10^5 CFU/mL of urine in baseline urine culture or the same bacterial pathogen present in concurrent blood and urine cultures. The Overall Response was a composite endpoint requiring clinical cure or improvement, and microbiological eradication (all baseline uropathogens at >10^5 were reduced to <10^4 CFU/mL).

This trial was designed to evaluate noninferiority with a pre-specified non-noninferiority margin of -15%. The efficacy results from Study 505 are summarized in Table 1.8,9 There was a statistically significant difference between the meropenem/vaborbactam success rate of 98.4% and the piperacillin/tazobactam rate of 94.0% with a difference in success rates of 4.5%, and the lower confidence limit of 0.7% for the difference exceeded zero. Based on this analysis, meropenem/vaborbactam appeared to be numerically superior to piperacillin/tazobactam at EOIVT visit.6

6 Section 505-1 (a) of the FD&C Act: FDAAA factor (C): The expected benefit of the drug with respect to such disease or condition.
Table 1: Study 505 Overall Response at EOIV (m-MITT population)\textsuperscript{8,9}

<table>
<thead>
<tr>
<th>Overall Response</th>
<th>Meropenem/Vaborbactam (n=192)</th>
<th>Meropenem/Vaborbactam (n=182)</th>
<th>Difference</th>
<th>95% CI</th>
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<tr>
<td>Success</td>
<td>189/192 (98.4%)</td>
<td>171/182 (94.0%)</td>
<td>4.5%</td>
<td>0.7% to 9.1%</td>
</tr>
<tr>
<td>Failure</td>
<td>2/192 (1.0%)</td>
<td>8/182 (4.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indeterminate</td>
<td>1/192 (0.5%)</td>
<td>3/182 (1.6%)</td>
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The key secondary end point was efficacy at test of cure (TOC). Success rates at the TOC visit were lower in both treatment groups as compared to the EOIVT visit; Overall Response of success at TOC was 74.5% for the meropenem/vaborbactam group and 70.3% for the piperacillin/tazobactam group with a difference of 4.1%, and lower limit of confidence interval of -4.9, meeting non-inferiority criteria. There was similar proportion of failures in both treatment groups at TOC (21.4% in meropenem/vaborbactam and 22% in piperacillin/tazobactam group), which were mainly due to recurrence of baseline pathogen.

5 Risk Assessment & Safe-Use Conditions

At the time of this writing, labeling negotiations were still ongoing with the Sponsor. The following section is a summary of relevant safety information to date for meropenem/vaborbactam. The key adverse events of special interest for meropenem-vaborbactam were identified based on the known safety profile of meropenem, and included pseudomembranous colitis/\textit{Clostridium difficile}-associated diarrhea (CDAD), hypersensitivity reactions, and seizures.\textsuperscript{1} Similar to the meropenem PI, the risk of breakthrough seizures due to drug interaction with valproic acid, development of drug-resistant bacteria, overgrowth of nonsusceptible organisms, thrombocytopenia, and the potential for neuromotor impairment will be communicated in the Warnings and Precautions section of the meropenem/vaborbactam label.

The safety analysis of meropenem/vaborbactam primarily focuses on 545 patients treated on Study 505 (272 patients treated with meropenem/vaborbactam and 273 patients treated with comparator piperacillin/tazobactam). Treatment was discontinued due to adverse reactions in 2.6% (7/272) of patients receiving meropenem/vaborbactam and in 5.1% (14/273) of patients receiving piperacillin/tazobactam. Most common adverse reactions resulting in discontinuation of meropenem/vaborbactam included hypersensitivity (n=2; 0.7%) and infusion-related reactions (n=2; 0.7%).

The integrated review of safety was based on the pooled results from two pooled data sets:

- The Phase 3 pool includes Study 505 and Study 506. In this pool, the piperacillin/tazobactam group in Study 505 and the Best Available Therapy (BAT) group in Study 506 were pooled into a

\textsuperscript{1} Section 505-1 (a) of the FD&C Act: FDAAA factor (E): The seriousness of any known or potential adverse events that may be related to the drug and the background incidence of such events in the population likely to use the drug.
single comparator group. This pooled data set includes 295 subjects treated with meropenem/vaborbactam and 289 subjects treated with a comparator.

- The All Treated Pool includes three Phase 1 clinical trials and Phase 3 trials (Study 501, 503, 504 and Study 505 and 506).

In Phase 3 trials, 545 patients received study treatment in Study 505, and of those 272 patients treated with the proposed dose of meropenem 2 g-vaborbactam 2 g. In Study 506, 39 patients were treated, and of those, 23 patients received the proposed dose of meropenem 2 g-vaborbactam 2 g.

Deaths

There were total of 12 deaths reported in the meropenem/vaborbactam development program. Four of the 12 deaths occurred in Study-505 (2 each in the meropenem/vaborbactam and piperacillin/tazobactam group), and the rest of 8 fatalities occurred in Study-506 (5 patients in the meropenem/vaborbactam group and 3 patients in the piperacillin/tazobactam group). In Study 505, death occurred in 2 (0.7%) patients who received meropenem/vaborbactam and in 2 (0.7%) patients who received piperacillin/tazobactam. Among meropenem/vaborbactam -treated patients, 1 patient died from aspiration and 1 patient died from sudden cardiac death. In Study 506, one patient died from multi-organ failure, one patient died from shock hemorrhagic, one patient died from cardiac arrest, and 2 patients died from septic shock. No deaths were considered to be related to the study drugs.9

Serious Adverse Events (SAE)

The incidence of any SAEs was similar between the meropenem/vaborbactam and comparator groups in Study 505, Phase 3 Pool and All treated Pool. In Study 505 there were 11 (4.0%), and 12 (4.4%) patients in the meropenem/vaborbactam group and comparator group, respectively, with any SAEs. In the Phase 3 Pool, the number of SAEs was 20 (6.8%) in the meropenem/vaborbactam group and 18 (6.2%) in the comparator group. Overall, frequencies of serious adverse events were similar in the Phase 3 pool (6.8% vs. 6.2%) and All Treated Pools (5.4% vs 5.3%) in the meropenem/vaborbactam and comparator groups, respectively.9

Treatment Emergent Adverse Events (TEAE)

The most frequent TEAEs in the Phase 3 Pool by preferred terms were headache, diarrhea, infusion-site phlebitis, and nausea. These were balanced between the two groups except for headaches. Similar results were seen in the All Treated Pool, which included headache, infusion-site phlebitis, diarrhea, infusion site pain, and nausea. Headache occurred at a ≥2% higher incidence in the meropenem/vaborbactam group than in the comparators group in both Phase 3 Pool and All Treated Pool. No severe headaches were reported and none of the headaches in either group were serious or resulted in discontinuation of study drug or discontinuation from the study.

Adverse Events of Special Interest

5.1 Hypersensitivity

The proportion of subjects with hypersensitivity reactions was similar in the meropenem/vaborbactam and comparator groups in both Phase 3 Pool (2.4% vs. 1.7%) and All Treated Pool (2.7% vs 2.1%).
Study 505, the hypersensitivity reactions led to discontinuation of study medication in 2 patients in the meropenem/vaborbactam group; and 3 patients in the comparator group. In Study 505, 2 infusion-related incidents occurred in the meropenem/vaborbactam group, which led to discontinuation of study drug. One patient had a life-threatening infusion-related reaction while undergoing infusion on study day 1, which led to discontinuation of study drug. It was assessed as serious and was considered probably related to study drug. A second patient had a severe infusion-related allergic reaction on study day 3 that led to discontinuation of the study drug. It was assessed as non-serious and was possibly related to study drug.9

The risk of hypersensitivity reactions will be included in Warnings and Precautions of the label.

5.2 SEIZURE

In both the Phase 3 and All Treated Pools, seizures were reported for no subject treated with meropenem/vaborbactam and 2 subjects (0.7%) treated with comparators. Both of these seizures were SAEs and occurred in Phase 3 Pool. One of these cases was considered severe, possibly related to the treatment with comparator, whereas the other case of seizure was considered unrelated to the comparator treatment. In both cases the SAEs were resolved.9

Although no cases of seizures were reported in the meropenem/vaborbactam group, warnings regarding seizures will be included in the Warnings and Precautions section of the label, similar to meropenem PI. Warnings regarding interaction with valproic acid will be included with instructions that antibacterial other than carbapenems should be considered to treat infections in patients whose seizures are well controlled on valproic acid or divalproex sodium.

5.3 PSEUDOMEMBRANOUS COLITIS/ Clostridium difficile-associated diarrhea (CDAD)

Clostridium difficile is a major causative agent of colitis and diarrhea associated with the use of antibacterial drugs. The proportion of patients with TEAEs in the category of CDAD was low and similar in the meropenem/vaborbactam and comparator groups in Phase 3 Pool (1 patient [0.3%] in the meropenem/vaborbactam group and 3 patients [1.0%], in comparator group); and in All treated Pool (1 patient [0.2%] in the mer-vab and 3 patients [0.9%], in comparator group).9

Similar to meropenem PI, the risk of C. difficile-associated diarrhea (CDAD) will be included in Warnings and Precautions of the label.

6 Expected Postmarket Use

According to the current proposed indication, if approved, meropenem/vaborbactam will be used both in inpatient and/or outpatient settings such as infusion centers or home infusion and will be prescribed by various types of healthcare providers such as general practice physicians, internal medicine physicians, midlevel practitioners, and Infectious Disease Specialists.
7 Risk Management Activities Proposed by the Applicant

The sponsor did not propose any risk management activities for meropenem/vaborbactam beyond routine pharmacovigilance and labeling. The sponsor proposed Prescribing Information (PI) that includes Warnings and Precautions to address the risks of hypersensitivity, seizures and *Clostridium difficile*-associated diarrhea.

8 Discussion of Need for a REMS

When evaluating factors of whether a REMS is necessary to ensure that the benefits outweigh the risks for meropenem/vaborbactam, DRISK considers patient population, seriousness of the disease, expected benefit of the drug, seriousness of known or potential adverse events, and the prescribing population.

Meropenem-vaborbactam is a combination product consisting of meropenem, a carbapenem-class antibacterial agent, and vaborbactam, a beta-lactamase inhibitor; proposed for indication as treatment of complicated urinary tract infections, including pyelonephritis. Based on the efficacy and safety information currently available, the clinical reviewer stated that application provided statistical evidence that meropenem/vaborbactam is effective for the treatment of complicated urinary tract infections, including acute pyelonephritis, and that it is noninferior to the comparator, piperacillin/tazobactam.

DRISK and DAIP have determined that if approved, a REMS is not necessary to ensure the benefits of meropenem/vaborbactam outweigh its risks. Labeling including Warnings and Precautions will be used to communicate the safety issues associated with meropenem/vaborbactam. Meropenem/vaborbactam demonstrated an overall favorable safety profile for the treatment of cUTI/pyelonephritis. The rates and frequencies of AEs were similar to what is known to occur when meropenem is used for other approved indications. The most common TEAEs were headache, diarrhea, infusion-site phlebitis, and nausea. Headache and infusion site inflammatory reactions were reported in a higher proportion of patients in the meropenem/vaborbactam group than in the comparator group. Although no significant safety signals were detected in this review, the meropenem/vaborbactam prescribing information will include safety information contained in the current meropenem label, in Warnings and Precautions. The most concerning adverse reactions associated with the use of meropenem/vaborbactam are hypersensitivity, seizures and *Clostridium difficile*-associated diarrhea.

A REMS is not necessary to ensure the benefits outweigh the risks of meropenem/vaborbactam for the following reasons:

- In the clinical trial, meropenem/vaborbactam appeared efficacious in both its primary and secondary outcomes. Meropenem-vaborbactam could provide an alternative treatment option as broad spectrum coverage for the treatment of cUTI/pyelonephritis, especially to address resistance in gram-negative bacteria due to KPC-producing CRE.

Warnings and Precautions in the meropenem/vaborbactam label will be included to address the risk of serious and occasionally fatal hypersensitivity (anaphylactic) reactions, as well as serious skin reactions. Warnings regarding seizures and other adverse CNS experiences will be included in the Warnings and Precautions section of the label. Warnings regarding interaction with valproic acid will be included with instructions that an antibacterial other than carbapenems should be considered to treat infections in patients whose seizures are well controlled on...
valproic acid or divalproex sodium. Similar to the meropenem PI, the risk of *C. difficile*-associated diarrhea (CDAD) will be included in Warnings and Precautions section of the label.

- The Centers for Disease Control and Prevention (CDC) recently issued guidelines for hospital stewardship programs. A core element is the appointment of a single pharmacist leader “responsible for working to improve antibiotic use”. Administration of meropenem/vaborbactam, an intravenously administered carbapenem antibacterial drug, occurs most often in a hospital setting, or occurs as an outpatient infusion where one would expect guidelines for antibiotic use to be utilized and in place, and also accompanied by appropriate monitoring by a pharmacist and other healthcare personnel. Other carbapenem antibacterial drugs with similar warnings and administered under similar inpatient and outpatient scenarios do not have a REMS requirement.

9 Conclusion & Recommendations

If approved, DRISK has determined that a REMS is not necessary to ensure the benefits outweigh its risks. The management of the risks associated with meropenem/vaborbactam treatment can be communicated through labeling. Please notify DRISK if new safety information becomes available that changes the benefit-risk profile; this recommendation can be reevaluated specifically REMS.

10 References

1 Proposed Prescribing Information for meropenem-vaborbactam as currently edited by the FDA, last updated June 12, 2017.


Centers for Disease Control and Prevention, Core Elements of Hospital Antibiotic Stewardship Programs, updated May 25, 2016.
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

TILL OLICKAL
06/27/2017

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06/27/2017