hikma.

Press Release

Hikma launches Meropenem for Injection, USP in the US

London, 14 January 2025 – Hikma Pharmaceuticals PLC (Hikma), the multinational pharmaceutical company, has launched Meropenem for Injection, USP in 500mg and 1g doses in the US. The product is indicated for:

- The treatment of complicated skin and skin structure infections (cSSSI) due to *Staphylococcus aureus* (methicillin-susceptible isolates only), *Streptococcus pyogenes, Streptococcus agalactiae*, viridans group streptococci, *Enterococcus faecalis* (vancomycin-susceptible isolates only), *Pseudomonas aeruginosa, Escherichia coli, Proteus mirabilis, Bacteroides fragilis,* and *Peptostreptococcus* species.

- The treatment of complicated appendicitis and peritonitis caused by viridans group streptococci, *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Bacteroides fragilis, B. thetaiotaomicron,* and *Peptostreptococcus* species.

- The treatment of bacterial meningitis caused by *Haemophilus influenzae, Neisseria meningitidis and penicillin-susceptible isolates of Streptococcus pneumoniae.* Meropenem for injection has been found to be effective in eliminating concurrent bacteremia in association with bacterial meningitis.

According to IQVIA, US sales of Meropenem for Injection, USP, 500mg and 1g, were approximately $61 million in the 12 months ending November 2024.

Hikma is a top three supplier of generic injectable medicines by volume in the US[1], with a growing portfolio of more than 170 products. We are continuously expanding our portfolio of essential medicines and introducing new dosage forms that enhance patient care.

- ENDS –

This product has been approved for marketing in the United States by the US FDA. This product approval does not confer the right on Hikma, or any other party, to market this product outside the United States.

Enquiries

Hikma Pharmaceuticals PLC

Susan Ringdal EVP, Strategic Planning and Global Affairs	+44 (0)20 7399 2760/ +44 7776 477050
Steven Weiss US Communications	+1 732 788 8279

[1] Source: IQVIA MAT November 2024, generic injectable volumes by eaches, excluding branded generics and Becton Dickinson

hikma.

About Hikma
(LSE: HIK) (NASDAQ Dubai: HIK) (OTC: HKMPY) (rated BBB-/stable S&P and BBB-/positive Fitch)

Hikma helps put better health within reach every day for millions of people around the world. For more than 45 years, we've been creating high-quality medicines and making them accessible to the people who need them. Headquartered in the UK, we are a global company with a local presence across North America, the Middle East and North Africa (MENA) and Europe, and we use our unique insight and expertise to transform cutting-edge science into innovative solutions that transform people's lives. We're committed to our customers, and the people they care for, and by thinking creatively and acting practically, we provide them with a broad range of branded and non-branded generic medicines. Together, our 9,100 colleagues are helping to shape a healthier world that enriches all our communities. We are a leading licensing partner, and through our venture capital arm, are helping bring innovative health technologies to people around the world. For more information, please visit: www.hikma.com

Important Safety Information for Meropenem for Injection, USP, 500mg and 1g:
Please see package insert for referenced section/section numbering, where appropriate.

CONTRAINDICATIONS

Meropenem for injection is contraindicated in patients with known hypersensitivity to any component of this product or to other drugs in the same class or in patients who have demonstrated anaphylactic reactions to beta (β)-lactams.

WARNINGS & PRECAUTIONS

- **Hypersensitivity Reactions –** Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients receiving therapy with β-lactams. These reactions are more likely to occur in individuals with a history of sensitivity to multiple allergens. There have been reports of individuals with a history of penicillin hypersensitivity who have experienced severe hypersensitivity reactions when treated with another β-lactam.
- **Severe Cutaneous Adverse Reactions –** Severe cutaneous adverse reactions (SCAR) such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), erythema multiforme (EM) and acute generalized exanthematous pustulosis (AGEP) have been reported in patients receiving meropenem.
- **Seizure Potential –** Seizures and other adverse CNS experiences have been reported during treatment with meropenem. These experiences have occurred most commonly in patients with CNS disorders (e.g., brain lesions or history of seizures) or with bacterial meningitis and/or compromised renal function.
- **Risk of Breakthrough Seizures Due to Drug Interaction with Valproic Acid –** The concomitant use of meropenem 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.
- ***Clostridium difficile*–associated Diarrhea –** *Clostridium difficile*-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including meropenem, and may range in severity from mild diarrhea to fatal colitis.
- **Development of Drug-Resistant Bacteria –** Prescribing meropenem in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.
- **Overgrowth of Nonsusceptible Organisms –** As with other broad-spectrum antibacterial drugs, prolonged use of meropenem may result in overgrowth of nonsusceptible organisms.
- **Thrombocytopenia –** In patients with renal impairment, thrombocytopenia has been observed but no clinical bleeding reported.
- **Potential for Neuromotor Impairment –** Alert patients receiving meropenem on an outpatient basis regarding adverse events such as seizures, delirium, headaches and/or paresthesias that could interfere with mental alertness and/or cause motor impairment. Until it is reasonably well established that meropenem is well tolerated, advise patients not to operate machinery or motorized vehicles.

ADVERSE REACTIONS

The following are discussed in greater detail in other sections of labeling:

- Hypersensitivity Reactions *[see Warnings and Precautions (5.1)]*
- Severe Cutaneous Adverse Reactions *[see Warnings and Precautions (5.2)]*
- Seizure Potential *[see Warnings and Precautions (5.3)]*
- Risk of Breakthrough Seizures Due to Drug Interaction with Valproic Acid *[see Warnings and Precautions (5.4)]*
- *Clostridium difficile* – associated Diarrhea *[see Warnings and Precautions (5.5)]*
- Development of Drug-Resistant Bacteria *[see Warnings and Precautions (5.6)]*
- Overgrowth of Nonsusceptible Organisms *[see Warnings and Precautions (5.7)]*
- Thrombocytopenia *[see Warnings and Precautions (5.8)]*
- Potential for Neuromotor Impairment *[see Warnings and Precautions (5.9)]*

Adverse Reactions from Clinical Trials
Because clinical trials are conducted under widely varying conditions, adverse reactions rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adult Patients
During clinical investigations, 2904 immunocompetent adult patients were treated for non-CNS infections with meropenem (500 mg or 1 gram every 8 hours). Deaths in 5 patients were assessed as possibly related to meropenem; 36 (1.2%) patients had meropenem discontinued because of adverse events. Many patients in these trials were severely ill and had multiple background diseases, physiological impairments and were receiving multiple other drug therapies. In the seriously ill patient population, it was not possible to determine the relationship between observed adverse events and therapy with meropenem. The following adverse reaction frequencies were derived from the clinical trials in the 2904 patients treated with meropenem.

Local Adverse Reactions
Local adverse events that were reported with meropenem were as follows:
Inflammation at the injection site 2.4%
Injection site reaction 0.9%
Phlebitis/thrombophlebitis 0.8%
Pain at the injection site 0.4%
Edema at the injection site 0.2%

Systemic Adverse Reactions
Systemic adverse events that were reported with meropenem occurring in greater than 1.0% of the patients were diarrhea (4.8%), nausea/vomiting (3.6%), headache (2.3%), rash (1.9%), sepsis (1.6%), constipation (1.4%), apnea (1.3%), shock (1.2%), and pruritus (1.2%). Additional systemic adverse events that were reported with meropenem and occurring in less than or equal to 1.0% but greater than 0.1% of the patients are listed in the package insert within each body system in order of decreasing frequency.

Complicated Skin and Skin Structure Infections
In a study of complicated skin and skin structure infections, the adverse reactions were similar to those listed in the package insert. The most common adverse events occurring in greater than 5% of the patients were: headache (7.8%), nausea (7.8%), constipation (7.0%), diarrhea (7.0%), anemia (5.5%), and pain (5.1%). Adverse events with an incidence of greater than 1%, and not listed above, include: pharyngitis, accidental injury, gastrointestinal disorder, hypoglycemia, peripheral vascular disorder, and pneumonia.

Patients with Renal Impairment
For patients with varying degrees of renal impairment, the incidence of heart failure, kidney failure, seizure and shock reported with meropenem, increased in patients with moderately severe renal impairment (creatinine clearance 10 to 26 mL/min).

Pediatric Patients
Pediatric Patients with Serious Bacterial Infections (excluding Bacterial Meningitis):
Meropenem was studied in 515 pediatric patients (3 months to less than 13 years of age) with serious bacterial infections (excluding meningitis, see next section) at dosages of 10 mg/kg to 20 mg/kg every 8 hours. The types of systemic and local adverse events seen in these patients were similar to the adults.

Pediatric Patients with Bacterial Meningitis:
Meropenem was studied in 321 pediatric patients (3 months to less than 17 years of age) with meningitis at a dosage of 40 mg/kg every 8 hours. The types of systemic and local adverse events seen in these patients were similar to the adults.

Pediatric Patients (Neonates and Infants less than 3 months of Age):
Meropenem was studied in 200 neonates and infants less than 3 months of age. The study was open-label, uncontrolled, 98% of the infants received concomitant medications, and the majority of adverse events were reported in neonates less than 32 weeks gestational age and critically ill at baseline, making it difficult to assess the relationship of the adverse events to meropenem.

Adverse Laboratory Changes in Pediatric Patients:
Laboratory changes seen in the pediatric studies, including the meningitis studies, were similar to those reported in the adult studies.

Post marketing Experience
The following adverse reactions have been identified during post-approval use of meropenem. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Worldwide post-marketing adverse reactions not otherwise listed in the Adverse Reactions from Clinical Trials section of this prescribing information and reported as possibly, probably, or definitely drug related are listed within each body system in order of decreasing severity.

Blood and Lymphatic System Disorders: agranulocytosis, neutropenia, and leukopenia; a positive direct or indirect Coombs test, and hemolytic anemia.
Immune System Disorders: angioedema.
Skin and Subcutaneous Disorders: Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS), erythema multiforme and acute generalized exanthematous pustulosis.

DRUG INTERACTIONS

Probenecid: Probenecid competes with meropenem for active tubular secretion, resulting in increased plasma concentrations of meropenem. Co-administration of probenecid with meropenem is not recommended.

Valproic Acid: 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.

USE IN SPECIFIC POPULATIONS

Pregnancy
Risk Summary
There are insufficient human data to establish whether there is a drug-associated risk of major birth defects or miscarriages with meropenem in pregnant women.

Lactation
Risk Summary
Meropenem has been reported to be excreted in human milk. No information is available on the effects of meropenem on the breast-fed child or on milk production.

Pediatric Use
The safety and effectiveness of meropenem have been established for pediatric patients 3 months of age and older with complicated skin and skin structure infections and bacterial meningitis, and for pediatric patients of all ages with complicated intra-abdominal infections.

Geriatric Use
Spontaneous reports and other reported clinical experience have not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Meropenem is known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with renal impairment. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Patients with Renal Impairment

Dosage adjustment is necessary in patients with creatinine clearance 50 mL/min or less.

DOSAGE AND ADMINISTRATION

Adult Patients

The recommended dose of meropenem for injection is 500 mg given every 8 hours for skin and skin structure infections and 1 gram given every 8 hours for intra-abdominal infections. When treating complicated skin and skin structure infections caused by *P. aeruginosa*, a dose of 1 gram every 8 hours is recommended.

Meropenem for injection should be administered by intravenous infusion over approximately 15 minutes to 30 minutes. Doses of 1 gram may also be administered as an intravenous bolus injection (5 mL to 20 mL) over approximately 3 minutes to 5 minutes.

Use in Adult Patients with Renal Impairment

Dosage should be reduced in patients with creatinine clearance of 50 mL/min or less. See dosing table 1 in package insert. There is inadequate information regarding the use of meropenem for injection in patients on hemodialysis or peritoneal dialysis.

Use in Pediatric Patients

Pediatric Patients 3 Months of Age and Older

- For pediatric patients 3 months of age and older, the meropenem for injection dose is 10 mg/kg, 20 mg/kg or 40 mg/kg every 8 hours (maximum dose is 2 grams every 8 hours), depending on the type of infection (cSSSI, cIAI, intra-abdominal infection or meningitis). See dosing table 2 in package insert.
- For pediatric patients weighing over 50 kg administer meropenem for injection at a dose of 500 mg every 8 hours for cSSSI, 1 gram every 8 hours for cIAI and 2 grams every 8 hours for meningitis.
- Administer meropenem for injection as an intravenous infusion over approximately 15 minutes to 30 minutes or as an intravenous bolus injection (5 mL to 20 mL) over approximately 3 minutes to 5 minutes.
- There is limited safety data available to support the administration of a 40 mg/kg (up to a maximum of 2 grams) bolus dose.

There is no experience in pediatric patients with renal impairment. When treating cSSSI caused by *P. aeruginosa*, a dose of 20 mg/kg (or 1 gram for pediatric patients weighing over 50 kg) every 8 hours is recommended.

Pediatric Patients Less Than 3 Months of Age

For pediatric patients (with normal renal function) less than 3 months of age, with complicated intra-abdominal infections, the meropenem for injection dose is based on gestational age (GA) and postnatal age (PNA). See dosing table 3 in package insert. Meropenem for injection should be given as intravenous infusion over 30 minutes. There is no experience in pediatric patients with renal impairment.

Preparation and Administration of Meropenem for Injection

Important Administration Instructions:

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

For Intravenous Bolus Administration

Re-constitute injection vials (500 mg and 1 gram) with sterile Water for Injection (see table 4 of package insert). Shake to dissolve and let stand until clear. Discard unused portion.

For Infusion

- Injection vials (500 mg and 1 gram) may be directly re-constituted with a compatible infusion fluid.
- Alternatively, an injection vial may be re-constituted, then the resulting solution added to an intravenous container and further diluted with an appropriate infusion fluid.
- Do not use flexible container in series connections.

Compatibility

Compatibility of meropenem for injection with other drugs has not been established. Meropenem for injection should not be mixed with or physically added to solutions containing other drugs.

Stability and Storage

Freshly prepared solutions of meropenem for injection should be used. However, reconstituted solutions of meropenem for injection maintain satisfactory potency under the conditions described below. Solutions of intravenous meropenem for injection should not be frozen.

Intravenous Bolus Administration
Meropenem for injection vials re-constituted with sterile Water for Injection for bolus administration (up to 50 mg/mL of meropenem for injection) may be stored for up to 3 hours at up to 25°C (77°F) or for 13 hours at up to 5°C (41°F).

Intravenous Infusion Administration
Solutions prepared for infusion (meropenem for injection concentrations ranging from 1 mg/mL to 20 mg/mL) re-constituted with Sodium Chloride Injection 0.9% may be stored for 1 hour at up to 25°C (77°F) or 15 hours at up to 5°C (41°F). Solutions prepared for infusion (meropenem for injection concentrations ranging from 1 mg/mL to 20 mg/mL) re-constituted with Dextrose Injection 5% should be used immediately.

OVERDOSAGE

Intentional overdosing of meropenem is unlikely, although accidental overdosing might occur if large doses are given to patients with reduced renal function. The largest dose of meropenem administered in clinical trials has been 2 grams given intravenously every 8 hours. At this dosage, no adverse pharmacological effects or increased safety risks have been observed.

Limited postmarketing experience indicates that if adverse events occur following overdosage, they are consistent with the adverse event profile described in the Adverse Reactions section and are generally mild in severity and resolve on withdrawal or dose reduction. Consider symptomatic treatments. In individuals with normal renal function, rapid renal elimination takes place. Meropenem and its metabolite are readily dialyzable and effectively removed by hemodialysis; however, no information is available on the use of hemodialysis to treat overdosage.

INDICATIONS AND USAGE

Complicated Skin and Skin Structure Infections (Adult Patients and Pediatric Patients 3 Months of Age and Older Only)
Meropenem for injection is indicated for the treatment of complicated skin and skin structure infections (cSSSI) due to *Staphylococcus aureus* (methicillin-susceptible isolates only), *Streptococcus pyogenes, Streptococcus agalactiae*, viridans group streptococci, *Enterococcus faecalis* (vancomycin-susceptible isolates only), *Pseudomonas aeruginosa, Escherichia coli, Proteus mirabilis, Bacteroides fragilis,* and *Peptostreptococcus* species.

Complicated Intra-abdominal Infections (Adult and Pediatric Patients)
Meropenem for injection is indicated for the treatment of complicated appendicitis and peritonitis caused by viridans group streptococci, *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Bacteroides fragilis, B. thetaiotaomicron,* and *Peptostreptococcus* species.

Bacterial Meningitis (Pediatric Patients 3 Months of Age and Older Only)
Meropenem for injection is indicated for the treatment of bacterial meningitis caused by *Haemophilus influenzae, Neisseria meningitidis and penicillin-susceptible isolates of Streptococcus pneumoniae.* Meropenem for injection has been found to be effective in eliminating concurrent bacteremia in association with bacterial meningitis.

Usage
To reduce the development of drug-resistant bacteria and maintain the effectiveness of meropenem for injection and other antibacterial drugs, meropenem for injection should only be used to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

HOW SUPPLIED/STORAGE AND HANDLING

Meropenem for Injection, USP is supplied in 20 mL and 30 mL injection vials containing sufficient meropenem to deliver 500 mg or 1 gram for intravenous administration, respectively. The dry powder should be stored at 20°C to 25°C (68°F to 77°F) [See USP Controlled Room Temperature].

500 mg Injection Vial (NDC 0143-9430-01)

Pack of 10 × 500 mg Injection Vials (NDC 0143-9430-10)
1 gram Injection Vial (NDC 0143-9431-01)
Pack of 10 × 1 g Injection Vials (NDC 0143-9431-10)

ENDING INFORMATION

Patient Counseling Information should be shared with the patient prior to administration.
For additional information, please refer to the Package Insert for full prescribing information, available on www.hikma.com.

To report SUSPECTED ADVERSE REACTIONS, contact Hikma Pharmaceuticals USA Inc. at 1-877-845-0689 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Manufactured by:
QILU Antibiotics Pharmaceutical Co., Ltd.

Manufactured for:
Hikma Pharmaceuticals USA Inc.
Berkeley Heights, NJ 07922 USA

Document Identification Number: HK-3206-v1