MPM
(Meropenem)
500mg / **1g** INJECTION
Powder for Solution for Infusion or Injection

ایم پی ایم
(میروپینم)
500 ملی گرام / **1** گرام انجیکشن

QUALITATIVE & QUANTITATIVE COMPOSITION
MPM I.V. (Meropenem) Powder for Solution for Infusion or Injection is available for parenteral administration as:
MPM I.V. 500mg
Each vial contains:
Meropenem trihydrate equivalent to meropenem USP 500mg
Blended with anhydrous Sodium Carbonate (Sterile)
MPM I.V. 1g
Each vial contains:
Meropenem trihydrate equivalent to meropenem USP 1g
Blended with anhydrous Sodium Carbonate (Sterile)
CLINICAL PHARMACOLOGY
Mechanism of Action
Meropenem exerts its bactericidal activity by inhibiting bacterial cell wall synthesis in Gram positive and Gram-negative bacteria through binding to penicillin-binding proteins (PBPs). Meropenem binds to PBPs 2, 3 and 4 of Escherichia coli and Pseudomonas aeruginosa; and PBPs 1,2 and 4 of Staphylococcus aureus
Pharmacokinetics
Absorption
Doses of 500mg. 1000mg and 2000mg of meropenem infused over 30minutes give mean Cmax values of approximately 23µg/mL, 49µg/mL and 115µg/mL respectively with corresponding AUC values of 39.3µg.h/mL, 62.3µg.h/mL and 153µg.h/mL. After infusion over 5 minutes Cmax values are 52µg/mL and 112µg/mL after 500mg and 1g doses respectively.
Distribution
The average plasma protein binding of meropenem is approximately 2% and is independent of concentration. Meropenem has been shown to penetrate well into several body fluids and tissues: including lung, bronchial secretions, bile, cerebrospinal fluid, gynaecological tissues, skin, fascia, muscle and peritoneal exudates.
Metabolism
Meropenem is metabolized by hydrolysis of the beta-lactam ring generating a microbiologically inactive metabolite.
Excretion
The elimination half-life of meropenem is approximately 1 hour. Meropenem is primarily excreted unchanged by the kidneys; approximately 70% (50-75%) of the dose is excreted unchanged within 12 hours. A further 28% is recovered as the microbiologically inactive metabolite fecal elimination represents only approximately 2% of the dose.
Special Population
Renal Impairment
Renal impairment results in higher plasma AUC and longer half-life for meropenem. There were AUC increases of 2.4 fold in patients with moderate impairment (CrCL 33-74ml/min), 5 fold in severe impairment (CrCL 4-23mL/min) and 10 fold in hemodialysis patients (CrCL <2ml/min) when compared to healthy patients (CrCL >80 ml/min).
Elderly Patients
Pharmacokinetic study with meropenem in elderly patients have shown a reduction in the plasma clearance of meropenem that correlates with age-associated reduction in creatinine clearance.
Pediatric population
Studies in children have shown that the pharmacokinetics of meropenem in children is essentially similar to those in adults. The elimination half-life for meropenem was approximately 1.5 hours in children under the age of 2 years.
The pharmacokinetics of meropenem in neonates requiring anti-infective treatment showed greater clearance in neonates with higher chronological or gestational age with an overall average half-life of 2.9 hours.

THERAPEUTIC INDICATIONS
MPM I.V. (Meropenem) is indicated for the treatment of the following infections in adults and children over 3 months of age:
• Severe pneumonia including hospital and ventilator-associated pneumonia
• Broncho-pulmonary infections in cystic fibrosis
• Complicated urinary tract infections
• Complicated intra-abdominal infections
• Intra- and post-partum infections
• Complicated skin and soft tissue infections
• Septicemia
• Management of febrile neutropenia
• Acute bacterial meningitis

DOSAGE AND ADMINISTRATION
The dose of MPM I.V. (Meropenem) administered and the duration of treatment should take into account the type of infection to be treated, including its severity and the clinical response.
A dose of up to 2g three times daily in adults and adolescents and a dose of up to 40mg/kg three times daily in children may be particularly appropriate when treating some types of infections, such as infections due to less susceptible bacterial species (e.g. Enterobacteriaceae, Pseudomonas aeruginosa or Acinetobacter spp.) or very severe infections.'
Adults and Adolescents

Infection	Dose to be administered every 8 hours
Severe pneumonia including hospital and ventilator-associated pneumonia	500mg to 1g
Complicated urinary tract infections	
Complicated intra-abdominal infections	
Intra-and post-partum infections	
Complicated skin and soft tissue infections	
Septicemia	
Management of febrile neutropenic patients	1g
Broncho-pulmonary infections in cystic fibrosis	2g
Acute bacteria! Meningitis	

Renal impairment
The dose for adults and adolescents should be adjusted with creatinine clearance of 50mL/min or less, as shown below:

Creatinine clearance (mL/min)	Dose (dependent on type of infection)	Dosing Interval
25-50	Recommended dose	Every 12 hours
10-25	One-half recommended dose	Every 12 hours
<10	One-half recommended dose	Every 24 hours

Meropenem is cleared by hemodialysis and hemofiltration. The required dose should be administered after completion of the hemodialysis cycle.
Pediatric population
Children from 3 months to 11 years of age and up to 50 kg body weight: The recommended dose regimens are shown in the table below:

Infection	Dose to be administered every 8 hours
Severe pneumonia including hospital and ventilator-associated pneumonia	10 to 20mg/kg
Complicated urinary tract infections	
Complicated intra-abdominal infections	
Complicated skin and soft tissue infections	
Septicemia	
Management of febrile neutropenic patients	20mg/kg
Broncho-pulmonary infections in cystic fibrosis	40mg/kg
Acute bacterial meningitis	

Children over 50 kg body weight:
The adult dose should be administered.
Directions for Use:
MPM I.V. (Meropenem) is usually given by intravenous infusion over approximately 15 to 30 minutes alternatively, doses of up to 20mg/kg can be given as an intravenous bolus injection over approximately 5 minutes.
Intravenous Injection:
Reconstitute MPM I.V, (Meropenem; vial with Sterile Water for Injection as per below table. Shake to dissolve and let stand until clear.

Product	Volume of Diluent added (mL)
MPM I.V. (Meropenem) 500mg	10mL
MPM I.V. (Meropenem) 1g	20mL

The reconstituted solution may be stored for 3 hours at up to 25°C or for 13 hours at 5°C.
Intravenous Infusion:
Reconstitute MPM I.V. (Meropenem) vial with Sterile Water for Injection as per below table. Shake to dissolve.

Product	Volume of Diluent added (mL)
MPM I.V. (Meropenem) 500mg	10mL
MPM I.V. (Meropenem) 1g	20mL

Further dilute the reconstituted solution with Sodium Chloride Solution for Infusion 0.9% or Dextrose Solution for Infusion 5%.
The Solution for Infusion (Meropenem concentrations ranging from 1mg/mL to 20mg/mL) prepared with Sodium Chloride Solution for infusion 0.9% may be stored for 1 hours at up to 25°C or for 15 hours at 5°C.
Reconstituted solution (Meropenem concentrations ranging from 1mg/mL to 20mg/mL) in Dextrose Solution for Infusion 5% should be used immediately.

Alternatively, MPM I.V. (Meropenem) may be directly reconstituted with a compatible infusion solution.

ADVERSE REACTIONS

Following adverse reactions have been reported during treatment with meropenem:

Common

Thrombocythemia, headache, diarrhea, vomiting, nausea, abdominal pain, increased transaminases, increased blood alkaline phosphatase, increased blood lactate dehydrogenase, rash, pruritis, inflammation and pain.

Uncommon

Oral and vaginal candidiasis, eosinophilia, thrombocytopenia, leucopenia, neutropenia, agranulocytosis, hemolytic anemia, angioedema, anaphylaxis, paraesthesiae, antibiotic-associated colitis, increased blood bilirubin, urticaria, toxic epidermal necrolysis, Stevens Johnson syndrome, erythema multiforme, Increased blood creatinine & urea, thrombophlebitis and pain at the injection site.

Rare

Convulsions.

CONTRAINDICATIONS

Meropenem is contraindicated in patients:

With known hypersensitivity to meropenem or to any excipient of the product. Hypersensitive to any other carbapenem antibacterial agent.

Who have demonstrated anaphylactic reactions to any other type of β-lactams antibacterial agent (e.g. Penicillins or cephalosporins).

PRECAUTIONS

- The selection of meropenem to treat an individual patient should take into account the appropriateness of using a carbapenem antibacterial agent based on factors such as severity of the infection, the prevalence of resistance to other suitable antibacterial agents and the risk of selecting for carbapenem-resistant bacteria.
- As with all beta-lactam antibiotics, serious and occasionally fatal hypersensitivity reactions have been reported. Before initiating therapy with meropenem, careful inquiry should be made concerning previous hypersensitivity reactions to beta-lactam antibiotics. If a severe allergic reaction occurs, meropenem should be discontinued and appropriate measures should be taken.
- Antibiotic-associated colitis and pseudomembranous colitis have been reported with nearly all anti-bacterial agents, including, meropenem, and may range in severity from mild to life threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea during or subsequent to the administration of meropenem. Discontinuation of therapy with meropenem and the administration of specific treatment for Clostridium difficile should be considered.
- Medicinal products that inhibit peristalsis should not be given.
- Seizures have infrequently been reported during treatment with carbapenems, including meropenem.
- Hepatic function should be closely monitored during treatment with meropenem due to the risk of hepatic toxicity (hepatic dysfunction with cholestasis and cytolysis).
- Patients with pre-existing liver disorders should have liver function monitored during treatment with meropenem.
- A positive direct or indirect Coombs test may develop during treatment with meropenem.
- Prolong use of meropenem may result in overgrowth of non-susceptible organisms. If superinfection does occur during therapy, appropriate measures should be taken.
- 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.
- 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.

Pregnancy

There are no adequate and well controlled studies in pregnant women. Meropenem should be used during pregnancy only if clearly needed.

Nursing Mother

Meropenem has been reported to be excreted in human milk. Caution should be exercised when meropenem is administered to a nursing mother.

DRUG INTERACTIONS

Probenecid

Probenecid competes with meropenem for active tubular secretion and thus inhibits the renal excretion of meropenem with the effect of increasing the elimination half-life and plasma concentration of meropenem. Caution is required if probenecid is co-administered with meropenem.

Valproic Acid

Decrease in blood levels of valproic acid have been reported when it is co-administered with carbapenem agents resulting in 60-100% decrease in valproic acid levels in about two days. If administration of meropenem is necessary, then supplemental anti-convulsant therapy should be considered.

Oral Anti-coagulants

Simultaneous administration of antibiotics with warfarin may augment its anti-coagulant effects. It Is recommended that the INR should be monitored frequently during and shortly after co-administration of antibiotics with an oral anti-coagulant agent.

OVER DOSAGE

Symptoms:

Adverse reactions following over dosage are consistent with the adverse reaction profile of meropenem and are generally mild in severity and resolve on withdrawal or dose reduction.

Treatment

Treatment of over dosage should be symptomatic. In individuals with normal renal function, rapid renal elimination will occur. Hemodialysis will remove meropenem and its metabolite.

STORAGE

Store at 25eC (Excursions permitted between 15°C to 30°C).

Protect from sunlight & moisture.

Do not freeze the reconstituted solution.

The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED

MPM I.V. (Meropenem) Powder for Solution for Injection or Infusion 500mg is available in pack of 1 vial with 10mL Sterile Water for Injection.

MPM I.V. (Meropenem) Powder for Solution for Infusion or Injection 1g is available in pack of 1 vial with 20ml Sterile Water for Injection.

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔ ۲۵ ڈگری سینٹی گریڈ تک رکھیں۔

محفوظ رکھنے کی حد ۱۵ سے ۳۰ ڈگری سینٹی گریڈ ہے۔ منجمد ہونے سے بچائیں۔

سورج کی روشنی اور نمی سے محفوظ رکھیں۔ تمام دوائیں بچوں کی پہنچ سے دُور رکھیں۔

انٹراوینس بولس:

۵۰۰ ملی گرام ۱۰ ملی لیٹر اسٹرائیل واٹر میں شامل کریں۔

۱ گرام، ۲۰ ملی لیٹر اسٹرائیل واٹر میں شامل کریں۔

دوا کی تیاری کے بعد:

۳ گھنٹے ۲۵ ڈگری سینٹی گریڈ اور ۱۳ گھنٹے ۵ ڈگری سینٹی گریڈ پر محفوظ رکھ سکتے ہیں۔

انٹراوینس انفیوژن:

0.9% سوڈیم کلورائیڈ سے تیار کردہ انفیوژن ایک گھنٹہ ۲۵ ڈگری سینٹی گریڈ اور ۱۵ گھنٹے ۵ ڈگری سینٹی گریڈ پر محفوظ رکھ سکتے ہیں۔

5% ڈیکسٹروس سے تیار کردہ انفیوژن کو فوری استعمال کرلیں۔

انجکشن میں کوئی غیر حل پذیر شے نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔

انتباہ: صرف رجسٹرڈ ڈاکٹر کے نسخہ پر فروخت کریں:

Marketed by: ATHIX Pvt Ltd

Manufactured by:
Nicholas Pharmaceuticals
Plot # 34, SS-2 National Industrial Zone Rawat, Islamabad-Pakistan.

Manufactured for:
Winlet Pharmaceuticals (Pvt.) Ltd.
30-Km, Lahore Sargodha Road, Sargodha.