105X412mm
7pt

Pospenem Powder for solution for injection 500mg
Pospenem Powder for solution for injection 1g

Active Substance(s)
- Pospenem 500mg : Meropenemtrihydrate 570mg equivalent to 500mg meropenem
- Pospenem 1g : Meropenemtrihydrate 1141mg equivalent to 1000mg meropenem

Product Description
Pospenem is a white or light yellowish white powder. Reconstitution solution is clear and varies from colorless to yellow depending on the concentration.

Pharmacodynamics
Meropenem is a carbapenem antibiotic for parenteral use, that is relatively stable to human dehydropeptidase-1 (DHP-1) and therefore, does not require the addition of an inhibitor of DHP-1. Meropenem exerts bactericidal activity by inhibiting cell wall synthesis by penetrating the cell wall of most gram-positive and gram-negative bacteria to reach penicillin-binding-protein (PBP) targets. Its strongest affinity is toward PBPs 2, 3, and 4 of Escherichia coli and Pseudomonas aeruginosa, and PBPs 1, 2, and 4 of Staphylococcus aureus. Bactericidal concentrations are typically one to two times the bacteriostatic concentrations; the exception is Listeria monocytogenes, against which lethal activity has not been observed. Similar to imipenem, the antibacterial action of meropenem is related to binding of the drug to penicillin binding proteins (PBPs) of gram-positive and gram-negative organisms. The high resistance of meropenem to most bacterial beta-lactamases and good penetration of the drug through the outer membrane also contribute significantly to antimicrobial activity. Meropenem may be less of an inducer of beta-lactamases than imipenem.

Pharmacokinetics
Absorption
Peak Concentration: dependent on dose, renal function, and administration technique. The time to peak concentration following intravenous administration is approximately 1 hour (range: 0.5 - 1.5 hours) after the start of the infusion
Distribution
Plasma protein binding of meropenem is approximately 2%. Meropenem achieves concentrations that match or exceed those required to inhibit most susceptible bacteria in most body fluids and tissues including cerebrospinal fluid. Peak concentrations in body fluids were mostly achieved in 1 hour following intravenous infusion. The volume of distribution is 12 to 20 L
Metabolism
Extrarenal, 20% to 25% increases up to 50% in patients with creatinine clearance of less than 20 mL/minute. There is one metabolite, which is inactive, ICI-213689
Elimination
Approximately 70% of a meropenem dose administered intravenously is recovered unchanged in the urine over 12 hours. The clearance of meropenem from plasma correlates with the creatinine clearance. There is no accumulation of repeated doses of meropenem 500 mg every 8 hours or 1 gram every 6 hours in patients with normal renal function. Dose adjustments are necessary in patients with renal impairment
Elimination Half-life
- Adults and children age 2 years and older: 1 hour
- Children age 3 months to 2 years : 1.5 hours
- Preterm neonates (27 to 32 weeks gestational age, 21 days mean postnatal age) : 3.4 hours
- Impaired renal function: 3.4 to 20 hours or longer

Indication
Pospenem is indicated for treatment, in adults and children, of the following infections caused by single or multiple bacteria sensitive to meropenem.
- Pneumonias and Nosocomial pneumonias
- Urinary Tract Infections
- Intra-abdominal Infections
- Gynaecological Infections, such as endometritis and pelvic inflammatory disease.
- Bacterial Meningitis
- Septicaemia
- Empiric treatment, for presumed infections in patients with febrile neutropenia, used as monotherapy or in combination with anti-viral or anti-fungal agents.

Pospenem has proved efficacious alone or in combination with other antimicrobial agents in the treatment of polymicrobial infections.

Recommended Dosage
The dosage and duration of therapy shall be established depending on type and severity of infection and the condition of the patient. The recommended daily dosage is as follows: 500 mg IV every 8 hours in the treatment of pneumonia, UTI and gynaecological infections such as endometritis. 1 g IV every 8 hours in the treatment of hospital acquired pneumonias, peritonitis, presumed infections in febrile neutropenic patients, septicaemia. As with other antibiotics, particular caution is recommended in using Pospenem as monotherapy in critically ill patients with known or suspected Pseudomonas aeruginosa lower respiratory tract infection.
Meningitis - the dose should be 2 g every 8 hours.
Regular sensitivity testing is recommended when treating Pseudomonas aeruginosa infection.

Dosage Schedule for Adults with Impaired Renal Function
Dosage should be reduced in patients with creatinine clearance less than 51 ml/min, as scheduled below :

Creatinine Clearance (ml/min)	Dose (based on unit doses of 500mg, 1g)	Frequency
26-50	one unit dose	every 12 hours
10-25	one-half unit dose	every 12 hours
<10	one-half unit dose	every 24 hours

Meropenem is cleared by haemodialysis. If continued treatment with Pospenem is necessary, it is recommended that the unit dose (based on the type and severity of infection) is administered at the completion of the haemodialysis procedure to restore therapeutically effective plasma concentrations.There is no experience in the use of Pospenem in patients undergoing peritoneal dialysis.
Hepatic Insufficiency
No dosage adjustment is necessary in patients with hepatic insufficiency
Elderly Patients
No dosage adjustment is required for the elderly with normal renal function or creatinine clearance values above 50 ml/min.
Children
For children over 3 months and up to 12 years of age the recommended dose is 10 - 20 mg/kg every 8 hours depending on type and severity of infection, susceptibility of the pathogen and the condition of the patient. In children over 50 kg weight, adult dosage should be used.
In meningitis the recommended dose is 40 mg/kg every 8 hours.
Febrile episodes in neutropenic patients-the dose should be 20mg/kg every 8 hours. There is no experience in children with renal impairment.

- ***Administration***

Pospenem can be given by IV bolus or IV infusion

- ***Compatibilities***

Pospenem may be constituted with compatible infusion fluids (50-200mL).
Pospenem is compatible with following infusion fluids: 0.9% Sodium chloride solution, 5% Dextrose solution, and Water for injection.
Pospenem should not be mixed with or added other drugs.

Mode of Administration
Pospenem can be given as bolus injection over approximately 5 minutes or by intravenous infusion over approximately 15-30 minutes. Pospenem to be used for IV bolus should be constituted with sterile water for injection (5mL per 250mg meropenem). This provides an approximate available concentration of 50mg/mL.
For IV infusion, Pospenem vials may be directly constituted with a compatible infusion fluid (as listed under Compatibilities) and then further diluted with the compatible infusion fluid, as needed.

Contraindication
- Anaphylactic reaction to beta-lactam antibiotics
- Hypersensitivity to any component of this product or to other drugs in the same class

Warnings and Precautions
There is some clinical and laboratory evidence of partial cross-allergenicity between other carbapenems and beta-lactam antibiotics, penicillins and cephalosporins. As with all beta-lactam antibiotics, rare hypersensitivity reactions have been reported. Before initiating therapy with Pospenem, careful inquiry should be made concerning previous hypersensitivity reactions to beta-lactam antibiotics. Pospenem should be used with caution in patients with such a history. If an allergic reaction to Pospenem occurs, the drug should be discontinued and appropriate measures taken.
Use of Pospenem in patients with hepatic disease should be made with careful monitoring of transaminase and bilirubin levels.
As with other antibiotics, overgrowth of non-susceptible organisms may occur and, therefore, continuous monitoring of each patient is necessary.
Use in infections caused by methicillin resistant staphylococci is not recommended.
Rarely, pseudomembranous colitis has been reported on Pospenem as with practically all antibiotics and may vary in severity from slight to life-threatening. Therefore, antibiotics should be prescribed with care for individuals with a history of gastro-intestinal complaints, particularly colitis.
It is important to consider the diagnosis of pseudomembranous colitis in the case of patients who develop diarrhoea in association with the use of Pospenem. Although studies indicate that a toxin produced by Clostridium difficile is one of the main causes of antibiotic-associated colitis, other causes should be considered.
The co-administration of Pospenem with potentially nephrotoxic drugs should be considered with caution.
Pospenem may reduce serum valproic acid levels. Sub-therapeutic levels may be reached in some patients.
Paediatric use : Efficacy and tolerability in infants under 3 months old have not been established; therefore, Pospenem is not recommended for use below this age. There is no experience in children with altered hepatic or renal function.
Effects on Ability to Drive and Use Machines
No data is available, but it is not anticipated that Pospenem will affect the ability to drive and use machines.
Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients receiving therapy with beta-lactams. Before initiating therapy with Pospenem, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, carbapenems or other beta-lactam agents. If an allergic reaction occurs, Pospenem must be discontinued immediately and appropriate alternative therapy instituted.

Interactions with other Medicaments
- Concurrent use of Pospenem and valproic acid may result in decreased valproic acid plasma concentrations and loss of anticonvulsant effect.
- Concurrent use of Pospenem and probenecid may result in increased plasma concentrations of meropenem
- Concurrent use of live typhoid vaccine and antibiotics may result in a decreased immunological response to the typhoid vaccine.

Statement on Usage During Pregnancy and Lactation
Pregnancy
The safety of Pospenem in human pregnancy has not been evaluated. Animal studies have not shown any adverse effect on the developing foetus. Pospenem should not be used in pregnancy unless the potential benefit justifies the potential risk to the foetus. In every case, it should be used under the direct supervision of the physician.
Lactation
Pospenem is detectable at very low concentrations in animal breast milk. Pospenem should not be used in breast-feeding women unless the potential benefit justifies the potential risk to the baby.

Adverse Effects / Undesirable Effects
- Immunologic Effects : rarely, systemic allergic reactions (hypersensitivity) which may include angioedema and manifestations of anaphylaxis.
- Dermatologic Effects : Thrombophlebitis, injection site pain & inflammation, rash, pruritus, urticaria, erythema multiforme, Stevens-Johnson Syndrome, toxic epidermal necrolysis.
- Gastro-intestinal Effects: abdominal pain, nausea, vomiting, diarrhoea.
- Hematologic Effects : Reversible thrombocythaemia, eosinophilia, thrombocytopenia, leucopenia and neutropenia(including very rare cases of agranulocytosis), haemolyticanaemia, bleeding.
- Hepatic Effects : Increases in serum concentrations of bilirubin, transaminases, alkaline phosphatase and lactic dehydrogenase alone or in combination.
- Central nervous system Effects : headache, paraesthesiae, seizure (convulsions)
- Other : Oral and vaginal candidosis.

Overdose and Treatment
Treatment is symptomatic and supportive. There is no known antidote. Rapid renal elimination will occur in patients without renal impairment. Hemodialysis will remove meropenem and its metabolite in patients with renal impairment.

Incompatibility
Compatibility of Pospenem with other drugs has not been established. Pospenem should not be mixed with or physically added to solutions containing other drugs. Freshly prepared solutions of Pospenem should be used whenever possible.

Storage Condition
The dry powder should be stored at below 30°C. Injection should not be frozen.The constituted solutions of Pospenem maintain satisfactory potency at 30°C or under refrigeration (4°C) as shown in the following table:

- Stability in Infusion vial

Diluents	Hours stable	
	30°C	4°C
0.9% NaCl	2	18
5% Dextrose	2	8
Water for Injection	2	24

- Stability in Plastic IV bag.

Diluents	Hours stable	
	30°C	4°C
0.9% NaCl	2	12
5% Dextrose	2	8
Water for Injection	2	24

Dosage Forms and Packaging Available
Pospenem Powder for solution for injection 500mg x 10's.;1g x 10's

Manufacturer
JW Pharmaceutical Corporation
56, Hanjin 1-gil, Songak-eup, Dangjin-si, Chungcheongnam-do, Republic of Korea

Product Registration Holder
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2019/04/24

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