Neopenem®

Meropenem USP

Presentation
Neopenem® 500 mg IV injection: Each vial contains sterile Meropenem Trihydrate USP 570.45 mg is equivalent to anhydrous Meropenem 500 mg.
Neopenem® 1 g IV injection: Each vial contains sterile Meropenem Trihydrate USP 1.14 g is equivalent to anhydrous Meropenem 1 g.

Mode of Action
Meropenem is a carbapenem antibiotic for parenteral use, that is stable to human dehydropeptidase-I (DHP-I). It is structurally similar to imipenem. Meropenem exerts its bactericidal action by interfering with vital bacterial cell wall synthesis. The ease with which it penetrates bacterial cells, its high level of stability to all serine β-lactamases and its marked affinity for the Penicillin Binding Proteins (PBPs) explain the potent bactericidal activity of Meropenem against a broad spectrum of aerobic and anaerobic bacteria. Meropenem is stable in susceptibility tests and these tests can be performed using the normal routine systems. In vitro tests show that Meropenem can act synergistically with various antibiotics. It has been demonstrated both in vitro and in vivo that Meropenem has a post-antibiotic effect against Gram-positive and Gram-negative organisms.

The in vitro antibacterial spectrum of Meropenem includes the majority of clinically significant Gram-positive and Gram-negative, aerobic and anaerobic strains of bacteria.

Indications
Neopenem® is indicated for treatment, in adults and children, of the following infections caused by single or multiple susceptible bacteria and as empiric therapy prior to the identification of the causative organisms:

- Lower Respiratory Tract Infections
- Urinary Tract Infections, including complicated infections
- Intra-abdominal Infections
- Gynaecological Infections, including postpartum infections
- Skin and Skin Structure Infections
- Meningitis
- Septicaemia
- Empiric treatment, including initital monotherapy, for presumed bacterial infections in host-compromised, neutropenic patient

Because of its broad spectrum of bactericidal activity against Gram-positive and Gram-negative aerobic and anaerobic bacteria, Neopenem® is effective for the treatment of polymicrobial infections.

Dosage and Administration
ADULTS:
Usual dose
500 mg to 1 g by intravenous administration every 8 hours depending on type and severity of infection, the known or expected susceptibility of the pathogen(s) and the condition of the patient.

Exceptions

1. Febrile episodes in neutropenic patients - the dose should be 1 g every 8 hours.
2. Meningitis - the dose should be 2 g every 8 hours.

As with other antibiotics, caution may be required in using Meropenem as monotherapy in critically ill patients with known or suspected *Pseudomonas aeruginosa* lower respiratory tract infections.

Regular sensitivity testing is recommended when treating *Pseudomonas aeruginosa* infections.

Neopenem® should be given as an intravenous bolus injection over approximately 5 minutes or by intravenous infusion over approximately 15 to 30 minutes (see Method of Administration).

ELDERLY
No dosage adjustment is required for the elderly with normal renal function or creatinine clearance values above 50 ml/min.

CHILDREN
For infants and children over 3 months and up to 12 years of age the recommended intravenous dose is 10 to 40 mg/kg every 8 hours depending on type and severity of infection, the known or suspected susceptibility of the pathogen(s) and the condition of the patient. In children over 50 kg weight, adult dosage should be used.

Exceptions

1. Febrile episodes in neutropenic patients - the dose should be 20 mg/kg every 8 hours.
2. Meningitis - the dose should be 40 mg/kg every 8 hours.

Neopenem® should be given as an IV bolus over approximately 5 minutes or by intravenous infusion over approximately 15 to 30 minutes.

There is no experience in children with renal impairment.

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 500 mg, 1 g, 2 g every 8 hours)	Frequency
26 to 50	one unit dose	every 12 hours
10 to 25	one-half unit dose	every 12 hours
<10	one-half unit dose	every 24 hours

Neopenem® is cleared by haemodialysis. If continued treatment with Neopenem® is necessary, the unit dose (based on the type and severity of infection) is recommended at the completion of the haemodialysis procedure to re-institute effective treatment.

Use in Adults with Hepatic Insufficiency
No dosage adjustment is necessary in patients with impaired hepatic metabolism.

Method of Administration
Neopenem® to be used for bolus intravenous injection should be constituted with sterile water for injection (10 mL per 500 mg meropenem). This provides an approximate available concentration of 50 mg/mL. Constituted solutions are clear or pale yellow.
Neopenem® for intravenous infusion may be directly constituted with a compatible infusion fluid and then further diluted (50 to 200 mL) with the compatible infusion fluid, as needed.
Neopenem IV is compatible with the following infusion fluids: 0.9% sodium chloride intravenous infusion, 5% or 10% glucose intravenous infusion, 5% glucose intravenous infusion with 0.02% sodium bicarbonate, 5% glucose and 0.9% sodium chloride intravenous infusion, 5% glucose with 0.225% sodium chloride intravenous infusion, 5% glucose with 0.15% potassium chloride intravenous infusion, 2.5% and 10% mannitol intravenous infusion.

Contraindications
Neopenem® is contraindicated in patients who have demonstrated hypersensitivity to this product.

Warnings and Precautions
Patients who have a history of hypersensitivity to carbapenems, penicillins or other beta-lactam antibiotics may also be hypersensitive to Neopenem®. As with all beta-lactam antibiotics rare hypersensitivity reactions have been reported.

Rarely, pseudomembranous colitis has been reported with Neopenem® as with virtually all antibiotics; therefore, its diagnosis should be considered in patients who develop diarrhoea in association with the use of Neopenem®.

Neopenem® may reduce serum valproic acid levels. Subtherapeutic levels may be reached in some patients.

Use in Children

Efficacy and tolerability in infants under 3 months old have not been established; therefore, Neopenem® is not recommended for use below this age.

Use in Patients with Liver Disease

Patients with pre-existing liver disorders should have liver function monitored during treatment with Neopenem®.

Use in Pregnancy & Lactation
Pregnancy category B. The safety of Neopenem® in human pregnancy has not been established, although animal studies have not shown an adverse effect on the developing foetus. Neopenem® should not be used in pregnancy unless the potential benefit justifies the potential risk to the foetus.
Meropenem is detectable at very low concentrations in animal breast milk. Neopenem® should not be used in breast-feeding women unless the potential benefit justifies the potential risk to the baby.

Adverse Effects
Neopenem® is generally well tolerated. Adverse events rarely lead to cessation of treatment. Serious adverse events are rare thrombocythaemia, nausea, vomiting, diarrhea, increases in serum transaminases, bilirubin, alkaline phosphatase, lactic dehydrogenase, inflammation, thrombophlebitis, pain, eosinophilia, thrombocytopenia, headache, paresthesiae, rash, urticaria, pruritis, leucopenia, neutropenia, agranulocytosis, convulsions, oral and vaginal candidiasis, haemolytic anaemia, angioedema, manifestations of anaphylaxis, pseudomembranous colitis, erythema multiforme, stevens-Johnson syndrome, toxic epidermal necrolysis.

Interactions
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. As the potency and duration of action of Neopenem® dosed without probenecid are adequate the co-administration of probenecid with Neopenem® is not recommended. The potential effect of Neopenem® on the protein binding of other medicines or metabolism has not been studied. However, the protein binding is so low (approximately 2%) that no interactions with other compounds would be expected on the basis of this mechanism.
Neopenem® has been administered concomitantly with many other medications without apparent adverse interaction. Neopenem® may reduce serum valproic acid levels. Subtherapeutic levels may be reached in some patients. However, no specific drug interaction studies other than with probenecid were conducted.

Overdosage
Intentional overdosing of Neopenem® is unlikely, although overdosing could occur during therapy particularly in patients with renal impairment. Limited post-marketing experience indicates that if adverse events occur following overdosage, they are consistent with the adverse event profile described in Adverse effects, are generally mild in severity and resolve on withdrawal or dose reduction. Symptomatic treatments should be considered. In normal individuals rapid renal elimination will occur. Haemodialysis will remove Neopenem® and its metabolite.

Special precautions for storage
Prior to constitution, store Neopenem® powder for intravenous injection or infusion packs below 25 °C. To reduce microbiological hazard, solutions of Neopenem® IV should be used as soon as practicable after reconstitution. The freshly reconstituted solution is recommended. Its efficacy is maintained for at least 2 hours at room temperature or 12 hours in the refrigerator at 2-8 °C. Solutions of Neopenem® should not be frozen.

Supply
Neopenem® 500 mg I.V Injection: Each combipack contains 1 vial of Meropenem Trihydrate USP 570.45 mg equivalent to anhydrous Meropenem 500 mg and 1 ampoule of 10 ml WFI.
Neopenem® 1 g I.V Injection: Each combipack contains 1 vial of Meropenem Trihydrate USP 1.14 g equivalent to anhydrous Meropenem 1 g and 1 ampoule of 20 ml WFI.

Medicine: Keep out of reach of children.

Healthcare

Manufactured for
Healthcare Pharmaceuticals Ltd.
by Popular Pharmaceuticals Ltd. Tongi.

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