Microorganisms

**DESCRIPTION**

Merogen I.V. (Meropenem) Powder for Solution for Injection or Infusion is a sterile, pyrogen-free, synthetic, broad-spectrum, carbapenem antibiotic for intravenous administration. Chemically, it is (4R,5S,6S)-3-[[(3S,5S)-5-(Dimethylcarbamoyl) dehydrogenase, rash, pruritis, inflammation and pain.

**Pharmacokinetics**

Doses of 500mg, 1000mg and 2000mg of meropenem infused over 30 minutes give mean Cmax values of approximately 33μg/mL, 66μg/mL and 110μg/mL respectively with corresponding mean AUC values of 330, 660 and 1100μg*h/mL respectively. The mean residence time is approximately 1 hour; the mean volume of distribution is approximately 287L/mL in 250mg falling to 30L/mL at 2g.

**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 within 12 hours. A further 28% is recovered as the microbiologically inactive metabolite. Oral elimination represents only approximately 2.5% of the dose. The measured renal clearance and the effect of probenecid show that meropenem undergoes both filtration and tubular secretion. Urinary concentrations of meropenem in excess of 10μg/mL are maintained for up to 5 hours after a 500 mg dose.

**Special Population**

**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 (Ccr 33-74 mL/min), 5 fold in severe impairment (Ccr 12-23 mL/min and 10 fold in hemodialysis patients (Ccr < 12 mL/min) when compared to healthy patients (Ccr > 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.

**THERAPEUTIC INDICATIONS**

Merogen 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

**DOSEAGE AND ADMINISTRATION**

The dose of Merogen 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**

<table>
<thead>
<tr>
<th>Infection</th>
<th>Dose to be administered every 8 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe pneumonia including hospital and ventilator-associated pneumonia</td>
<td>500mg to 1g</td>
</tr>
<tr>
<td>Complicated urinary tract infections</td>
<td></td>
</tr>
<tr>
<td>Complicated intra-abdominal infections</td>
<td></td>
</tr>
<tr>
<td>Intra- and post-partum infections</td>
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<td>Septicemia</td>
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</tr>
<tr>
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<td>1g</td>
</tr>
<tr>
<td>Broncho-pulmonary infections in cystic fibrosis</td>
<td></td>
</tr>
<tr>
<td>Acute bacterial meningitis</td>
<td>2g</td>
</tr>
</tbody>
</table>

**Hand resection**

The dose for adults and adolescents should be adjusted with creatinine clearance of 30mL/min or less, as shown below:

- 500mg to 1g
- 333mg to 500mg
- 250mg to 333mg
- 200mg to 250mg
- 100mg to 125mg
Mycoplasma pneumoniae
Chlamydia psittaci
Chlamydia pneumoniae
Enterococcus faecium
Prevotella disiens
Bacteroides fragilis
Gram-negative anaerobes
(Proteus vulgaris
Morganella morganii
Citrobacter freudii
S. intermedius)

and Staphylococcus species

-3-pyrrolidinyl] thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-1-azabicyclo[3.2.0]pyrroren-free, synthetic, broad-spectrum, carbapenem antibiotic for intravenous

DESCRIPTION

Microbiology

Each vial contains:
Meroget I.V. 1g

CLINICAL PHARMACOLOGY

Intravenous injection
Reconstitute Meroget I.V. (Meropenem) vial with Sterile Water for Injection as per below table. Shake to dissolve and let stand until clear.

<table>
<thead>
<tr>
<th>Product</th>
<th>Volume of Diluent added (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meroget I.V. (Meropenem) 500mg</td>
<td>10mL</td>
</tr>
<tr>
<td>Meroget I.V. (Meropenem) 1g</td>
<td>20mL</td>
</tr>
</tbody>
</table>

The reconstituted solution may be stored for 3 hours at up to 25°C or for 12 hours at 2-8°C.

Intravenous infusion
Reconstitute Meroget I.V. (Meropenem) vial with Sterile Water for Injection as per below table. Shake to dissolve.

<table>
<thead>
<tr>
<th>Product</th>
<th>Volume of Diluent added (mL)</th>
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</thead>
<tbody>
<tr>
<td>Meroget I.V. (Meropenem) 500mg</td>
<td>10mL</td>
</tr>
<tr>
<td>Merigel I.V. (Meropenem) 1g</td>
<td>20mL</td>
</tr>
</tbody>
</table>

Further dilute the reconstituted solution with Sodium Chloride Solution for Infusion 0.9% or Dextrose Solution for Infusion 5% to obtain final concentrations ranging from 1mg/mL to 20mg/mL. Prepared with Sodium Chloride Solution for Infusion 0.9% or Dextrose Solution for Infusion 5% for 10mL to 20mL (for 12 hours at 2-8°C) or for 24 hours at 25°C.

Reconstituted solution (Meropenem concentrations ranging from 1mg/mL to 20mg/mL) in Dextrose Solution for Infusion 5% should be used immediately.

Alternatively, Meropenem 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
Thrombocytopenia, headache, dizziness, vomiting, nausea, abdominal pain, increased transaminases, increased blood alkaline phosphatase, increased blood lactate dehydrogenase, rash, pruritus, inflammation and pain.

Uncommon
Oral and vaginal candidiasis, eosinophilia, thrombocytopenia, leukopenia, neutropenia, agranulocytosis, hemolytic anemia, angioedema, anaphylaxis, pancreatitis, 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
Cocaine

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 beta-lactam 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 allergy reaction occurs, meropenem should be discontinued and appropriate therapy should be taken.
- Antibiotic-associated colitis and pseudomembranous colitis have been reported with nearly all antibacterial 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 platelets should not be given.
- Seizures have infrequently been reported during treatment with carbapenems, including meropenem.

ADVERSE EFFECTS

- Hepatic function should be closely monitored during treatment with meropenem due to the risk of hepatic toxicity (hepatic dysfunction, cholestasis and cholestasis).
- 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.
- Prolonged use of meropenem may result in overgrowth of non-susceptible flora. 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 in 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 urticaria, delirium, headaches and/or paresthesia 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 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 observed when it is co-administered with carbapenem agents resulting in 50-100% decrease in valproic acid levels in about 2 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.

OVERDOSAGE

- Adverse reactions following overdosage 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 overdose should be symptomatic. In individuals with normal renal function, rapid renal elimination will occur. Hemodialysis will remove meropenem and its metabolites.

STORAGE

- Store at 25°C (Excursions permitted between 10°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

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

Meroget I.V. (Meropenem) Powder for Solution for Infusion or Injection 1g is available in pack of 1 vial with 2x10mL, Sterile Water for Injection.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use. This package insert is continually updated from time to time.

Manufactured by:
Shenzhen Hubin Pharmaceutical Co., Ltd.
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Manufactured for:

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