Meropenem
Newborn Use Only

Alert
The Antimicrobial Stewardship Team recommends this drug is listed under the following category: Restricted. Widespread use of carbapenems has been linked with increasing prevalence of infections caused by methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE), multi-resistant Gram-negative organisms and Clostridium difficile.

Indication
Severe infections (e.g., sepsis or meningitis) caused by Gram-negative organisms resistant to other conventional antibiotics but susceptible to meropenem e.g., Extended Spectrum Beta Lactamase (ESBL)-producing organisms. Note: Meropenem is NOT active against many susceptible Gram-positive organisms, such as MRSA and most Staphylococcus epidermidis. Vancomycin is first-line therapy for these. Meropenem does have activity against penicillin-susceptible Gram-positive organisms and most anaerobic organisms. For individual advice, discuss therapy with a microbiologist or infectious diseases physician.

Action
Meropenem is a carbapenem. It inhibits cell wall synthesis. Meropenem is a better choice than imipenem for central nervous system infections. Meropenem attains a higher concentration in the cerebrospinal fluid particularly with inflamed meninges and has a lower incidence of seizures than imipenem.

Drug Type
Carbapenem antibiotic.

Trade Name
Meropenem APOTEX, Meropenem DBL, Meropenem Kabi, Meropenem Ranbaxy, Meropenem Sandoz, Merrem

Presentation
500 mg vial
1000 mg vial

Dosage / Interval

<table>
<thead>
<tr>
<th>Non-CNS Sepsis</th>
<th>Gestational Age at birth</th>
<th>Postnatal Age</th>
<th>Dose</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 32^{nd} weeks</td>
<td>0–13 days</td>
<td>20 mg/kg</td>
<td>12 hourly</td>
<td></td>
</tr>
<tr>
<td>&lt; 32^{nd} weeks</td>
<td>14+ days</td>
<td>20 mg/kg</td>
<td>8 hourly</td>
<td></td>
</tr>
<tr>
<td>≥ 32^{nd} weeks</td>
<td>0–13 days</td>
<td>20 mg/kg</td>
<td>8 hourly</td>
<td></td>
</tr>
<tr>
<td>≥ 32^{nd} weeks</td>
<td>14+ days</td>
<td>30 mg/kg</td>
<td>8 hourly</td>
<td></td>
</tr>
</tbody>
</table>

*Meningitis and Pseudomonas Sepsis*

<table>
<thead>
<tr>
<th>Gestational Age at birth</th>
<th>Postnatal Age</th>
<th>Dose</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>Any</td>
<td>40 mg/kg</td>
<td>8 hourly</td>
</tr>
</tbody>
</table>

*Assess for any renal impairment prior to using higher doses as meropenem is primarily excreted via the kidneys.

Route
IV infusion.

Maximum Daily Dose

Preparation/Dilution
Add 9.6 mL of WFI to the 500 mg powder for reconstitution to make a volume of 10 mL with a concentration of 50 mg/mL. Draw up 2 mL (100 mg of meropenem) of solution and add 8 mL sodium chloride 0.9% to make a final volume of 10 mL with a concentration of 10 mg/mL.

Larger doses or neonates with a fluid restriction
Add 9.6 mL of WFI to the 500 mg powder for reconstitution to make a volume of 10 mL with a concentration of 50 mg/mL. Draw up 4 mL (200 mg of meropenem) of solution and add 6 mL sodium chloride 0.9% to make a final volume of 10 mL with a concentration of 20 mg/mL.

Administration
IV infusion over 15 minutes.

Monitoring
Monitor renal function. Dose may need to be adjusted in impaired renal function.
## Contraindications
Hypersensitivity to penicillins, cephalosporins and carbapenems.

## Precautions
Colitis—due to risk of pseudomembranous colitis.
Renal impairment.

## Drug Interactions
Sodium valproate—meropenem may result in clinically significant reduction in concentration of sodium valproate, which may cause seizures.

## Adverse Reactions
Injection site inflammation, diarrhoea (up to 6% in children), anaemia and eosinophilia.

## Compatibility
**Fluids:** Glucose 5%, glucose 10%, sodium chloride 0.9%.
**Y-site:** Amino acid solutions, anidulafungin, caspofungin, linezolid, atropine sulfate monohydrate, dexamethasone sodium, gentamicin, heparin sodium, metronidazole.

## Incompatibility
**Fluids:** No information
**Y-site:** Dolasetron, ketamine, mycophenolate mofetil, zidovudine.

## Stability
**Merrem:** Solutions in sodium chloride are stable for 3 hours below 25°C and 24 hours at 2–8°C. Use solutions in glucose 5% immediately.
**Meropenem (DBL, Kabi, Ranbaxy, Sandoz):** Solutions in sodium chloride are stable for 8 hours below 25°C and 24 hours at 2–8°C. Solutions in glucose 5% are stable for 3 hours below 25°C and 14 hours at 2–8°C. Diluted solutions are potentially unstable, particularly glucose containing solutions and should be discarded if not used immediately.

## Storage
Vial: Store at room temperature.

## Special Comments
Meropenem 1 g vial contains 3.92 mmol of sodium.

## Evidence summary
**Efficacy:**
Carbapenems may be considered the treatment of choice for empirical treatment of patients with ESBL-producing *Enterobacteriaceae* bacteraemia. A systematic review of carbapenems for the treatment of patients with extended-spectrum β-lactamase (ESBL)-positive *Enterobacteriaceae* bacteraemia involving 1584 patients, mostly adults showed lower mortality than non-Beta-lactam/Beta-Lactam Inhibitor combination antibiotics for definitive [risk ratio (RR) 0.65, 95% CI 0.47–0.91] and empirical (RR 0.50, 95% CI 0.33–0.77) treatment. No statistically significant differences in mortality were found between carbapenems and BL/BLIs administered as definitive (RR 0.52, 95% 0.23–1.13) or empirical (RR 0.91, 95% CI 0.66–1.25) treatment (LOE 1, GOR C) [1].

A retrospective case series of 100 neonates infected by extended-spectrum beta-lactamase-producing *Klebsiella* species showed higher mortality in those neonates not started on empirical meropenem or Piperacillin + tazobactam and amikacin (OR – 17.01, 95% CI 2.41–120.23) (LOE IV, GOR C) [2].

**Pharmacokinetics:**
Meropenem is primarily excreted via the kidneys.
Meropenem clearance is influenced by serum creatinine and postmenstrual age in neonates [1].

A comparative pharmacokinetic study of short (30 minute) versus long (4 hour) infusion in neonates showed short infusion resulted in a higher mean drug concentration in serum (C(max)) than a prolonged infusion [3].

There is a knowledge gap in pharmacokinetic (PK) studies of neonates with renal impairment [1,2]. However, dose adjustment for renal failure may not be appropriate in cases where severe sepsis is probably responsible for acute renal failure [expert opinion].

**Dose:**
Multicentre, prospective PK study conducted in USA suggested a dosing strategy of 20 mg/kg every 12 hours in infants < 32 weeks GA and PNA < 14 days; 20 mg/kg every 8 hours in infants < 32 weeks GA and PNA ≥ 14 days and in infants ≥ 32 weeks GA and PNA < 14 days; and 30 mg/kg every 8 hours in infants ≥ 32 weeks GA and PNA ≥ 14 days to achieve therapeutic concentrations in
infants with suspected intra-abdominal infections [3].

References