### 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 resistant 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

#### Non-CNS 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>&lt; 32&lt;sup&gt;th&lt;/sup&gt; weeks</td>
<td>0–13 days</td>
<td>20 mg/kg</td>
<td>12 hourly</td>
</tr>
<tr>
<td>&lt; 32&lt;sup&gt;th&lt;/sup&gt; weeks</td>
<td>14+ days</td>
<td>20 mg/kg</td>
<td>8 hourly</td>
</tr>
<tr>
<td>≥ 32&lt;sup&gt;th&lt;/sup&gt; weeks</td>
<td>0–13 days</td>
<td>20 mg/kg</td>
<td>8 hourly</td>
</tr>
<tr>
<td>≥ 32&lt;sup&gt;th&lt;/sup&gt; weeks</td>
<td>14+ days</td>
<td>30 mg/kg</td>
<td>8 hourly</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-lactamases (ESBL)-positive *Enterobacteriaceae* bacteraemia involving 1584 patients, mostly adults showed lower mortality than non-β-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**
2. Velaphi S, Wadula J, Nakwa F. Mortality rate in neonates infected with extended-spectrum b-

Original version Date: 05/12/2015
Current Version number: 1.1
Risk Rating: Medium
Approved by: As per Local policy

Author: NeoMed Consensus Group
Version Date: 20/02/2017
Due for Review: 20/02/2020
Approval Date: As per Local policy

This is a printed copy. Refer to Neomed electronic system for the most up to date version.