**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. (1)

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 GH, Meropenem Juno, Meropenem Kabi, Meropenem Sandoz, Merrem

**Presentation**
500 mg vial
1000 mg vial

**Dose**

<table>
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<tr>
<th>Non-CNS and Non-Pseudomonas Sepsis</th>
<th>Gestational Age at birth</th>
<th>Postnatal Age</th>
<th>Dose</th>
<th>Interval</th>
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</thead>
<tbody>
<tr>
<td>&lt; 32(^{th}) weeks</td>
<td>0–13 days</td>
<td>20 mg/kg</td>
<td>12 hourly</td>
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<tr>
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<td>14+ days</td>
<td>20 mg/kg</td>
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<tr>
<td>≥ 32(^{th}) weeks</td>
<td>0–13 days</td>
<td>20 mg/kg</td>
<td>8 hourly</td>
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<tr>
<td>≥ 32(^{th}) weeks</td>
<td>14+ days</td>
<td>30 mg/kg</td>
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<th>Meningitis and Pseudomonas Sepsis</th>
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<td>Any</td>
<td>40 mg/kg</td>
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**Dose adjustment**
Assess for renal impairment prior to using higher doses as meropenem is primarily excreted via kidneys.

**Maximum dose**

**Total cumulative dose**

**Route**
IV infusion.

**Preparation**

**Infants <1 kg**
Add 9.6 mL of water for injection to 500 mg vial to make a 50 mg/mL solution OR Add 19.1 mL of water for injection to 1g vial to make a 50 mg/mL solution.

**FURTHER DILUTE**
Draw up 2 mL (100 mg of meropenem) of the above solution and add 8 mL sodium chloride 0.9% to make a final volume of 10 mL with a final concentration of 10 mg/mL.

**Infants ≥1 kg or fluid restricted**
Add 9.6 mL of water for injection to 500 mg vial to make a 50 mg/mL solution OR Add 19.1 mL of water for injection to 1g vial to make a 50 mg/mL solution.

**FURTHER DILUTE**
Draw up 4 mL (200 mg of meropenem) of the above 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 4 hours. (5)
May be given over 15 to 30 minutes if longer infusion time is not feasible.

**Monitoring**
Renal function.
Liver function.
Electrolytes
Meropenem
Newborn use only

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
Phlebitis, diarrhoea (up to 6% in children), anaemia and eosinophilia.

Compatibility
Fluids: sodium chloride 0.9% (preferred for stability), glucose 5%, glucose 10%,
Y-site: Amino acid solutions, anidulafungin, caspofungin, linezolid, atropine, dexamethasone sodium,
gentamicin, heparin sodium, metronidazole.

Incompatibility
Fluids: Mannitol 10%
Y-site: Dolasetron, ketamine, zidovudine.

Stability
Use immediately after preparation.
Diluted solutions are potentially unstable, particularly glucose containing solutions and should be discarded if not used immediately.

Storage
Vial: Store at room temperature.

Excipients
Sodium carbonate

Special comments
Meropenem 1 g vial contains 3.92 mmol of sodium.

Evidence

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).

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).

A RCT reported a prolonged infusion (4 hours) of meropenem (20 mg/kg/dose every 8 hours and 40 mg/kg/dose every 8 hours in meningitis and Pseudomonas infection) in 102 neonates with gram-negative late onset infection is associated with higher rate of clinical improvement, microbiologic eradication, less neonatal mortality (14% versus 31%; p=0.03), shorter duration of respiratory support and less acute kidney injury compared with the conventional strategy (30 minute infusion) [LOE II GOR B].

Pharmacokinetics:
Meropenem is primarily excreted via the kidneys.
Meropenem clearance is influenced by serum creatinine and postmenstrual age in neonates.
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. However, a longer infusion may have greater efficacy.5
There is a knowledge gap in pharmacokinetic (PK) studies of neonates with renal impairment.2,3
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.
## References


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