Alert
High risk medicine.
Antimicrobial Stewardship Team recommends this drug is listed as 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*.
NOT the preferred carbapenem in neonates because of possible adverse effects. Should be avoided in preterm neonates because of cilastatin accumulation.

Indication
Non-CNS sepsis caused by susceptible organisms including enteric Gram-negative rods, extended-spectrum beta-lactamase (ESBL) organisms, *Pseudomonas aeruginosa*, anaerobic organisms (including *Bacteroides fragilis*) and many Gram-positive organisms.

Action
Inhibits cell wall synthesis. Cilastatin prevents renal metabolism of imipenem.
Meropenem is a better choice for central nervous system infections as it attains a higher concentration in the cerebrospinal fluid and has a lower incidence of seizures than imipenem + cilastatin.

Drug type
Carbapenem antibiotic

Trade name
Primaxin

Presentation 500 mg vial.

Dose
Dose based on imipenem component

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose</th>
<th>Dosing Interval</th>
<th>Infusion Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-<em>Pseudomonas aeruginosa</em></td>
<td>25 mg/kg</td>
<td>12 hourly</td>
<td>30 minutes</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>25 mg/kg</td>
<td>8 hourly</td>
<td>90 minutes</td>
</tr>
</tbody>
</table>

Dose adjustment
Dose may need to be reduced in impaired renal function.

Maximum dose 75 mg/kg/day

Total cumulative dose

Route
IV Infusion

Preparation
Add 9.2 mL of sodium chloride 0.9% to the 500 mg vial to make a 50 mg/mL solution
FURTHER DILUTE
Draw up 3 mL (150 mg of Imipenem component) of the above solution and add 27 mL sodium chloride 0.9% to make a final volume of 30 mL with a final concentration of 5 mg/mL.*(10,11)
*Higher concentrations (10 mg/mL) may be used in fluid restricted neonates preferably via central line (ANMF consensus)

Administration
Non-*Pseudomonas aeruginosa* – IV infusion over 30 minutes.
*Pseudomonas aeruginosa* – IV infusion over 90 minutes.

Monitoring
Renal function. Dose may need to be reduced in impaired renal function.
Blood count and liver function.

Contraindications
Hypersensitivity to penicillins, cephalosporins or carbapenems.
CNS infections.

Precautions
Seizures can occur in infants with renal impairment or central nervous system infection.

Drug interactions
Ganciclovir – risk of seizures. Do not give concomitantly unless the potential benefits outweigh the risks.
Valproate – results in decreased concentrations of valproate.

Adverse reactions
Seizures, impaired renal function, impaired liver function, tachycardia, local phlebitis, urticaria, diarrhoea, pseudomembranous colitis (*Clostridium difficile*) and vomiting.

Compatibility
Fluids (10): Glucose 5%, glucose 10%, sodium chloride 0.9%
Y-site (10): Aciclovir, aztreonam, caspofungin, cisatracurium, foscarnet, linezolid, remifentanil, tigecycline, zidovudine.

Incompatibility
Fluids (10): Hartmann’s.
Y-site (10): Amiodarone, amoxicillin, azathioprine, azithromycin, ceftriaxone, daptomycin, ganciclovir, metaraminol, midazolam, milrinone, pyridoxine, sodium bicarbonate, thiamine, vecuronium.

Stability
Reconstituted or diluted solution stable for 4 hours below 25°C or for 24 hours at 2–8°C.

Storage
Store vial below 25°C.

Excipients
Sodium bicarbonate
### Imipenem-cilastatin

#### Newborn use only

<table>
<thead>
<tr>
<th>Special comments</th>
<th>Solutions of imipenem + cilastatin range from colourless to yellow. Variations of colour within this range do not affect the potency.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Evidence</strong></td>
<td><strong>Pharmacokinetics</strong> Imipenem-cilastatin is excreted via kidneys, mainly though glomerular filtration. Imipenem clearance is not influenced by postnatal or postmenstrual age. Infusions (0.5 hours) of 25 mg/kg every 12 hours (50 mg/kg/day) is sufficient against common bacterial isolates in neonates. However, 1.5 hour infusions of 25 mg/kg every 8 hours (75 mg/kg/day) in neonates are required to be effective against <em>Pseudomonas aeruginosa.</em> (1) <strong>Safety:</strong> Seizures can occur in neonates with meningitis, other CNS infections and in patients with renal impairment. (1,4,6,9)</td>
</tr>
<tr>
<td><strong>Practice points</strong></td>
<td></td>
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<table>
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<td>12/11/2020</td>
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<td>Current 3.0</td>
<td>3/04/2021</td>
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<td>REVIEW</td>
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- **Nursing Review** Eszter Jozsa, Kirsty Minter, Samantha Hassall
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- **Facilitator** Srinivas Bolisetty

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**ANMF consensus group** Imipenem-cilastatin Page 2 of 2