## Alert

Imipenem + cilastatin is not the preferred carbapenem in neonates because of possible adverse effects and should be avoided in preterm neonates because of cilastatin accumulation.

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

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

Imipenem + cilastatin is a carbapenem. It inhibits cell wall synthesis. Imipenem is combined with cilastatin. Cilastatin prevents renal metabolism of imipenem.

Meropenem is a better choice than imipenem + cilastatin for central nervous system infections. Meropenem 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.

## Dosage / Interval

<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>

## Route

IV Infusion.

## Maximum Daily Dose

75 mg/kg/day

## Preparation/Dilution

Add 9.2 mL of sodium chloride 0.9% to the 500 mg powder for reconstitution to make a volume of 10 mL with a concentration of 50 mg/mL (Note: Suspension maybe cloudy).

Draw up 1 mL (50 mg) and add 9 mL sodium chloride 0.9% to make a final volume of 10 mL with a concentration of 5 mg/mL.

## Administration

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

*Pseudomonas aeruginosa* – IV infusion over 90 minutes.

## Monitoring

Monitor renal function. Dose may need to be reduced in impaired renal function. Monitor 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.
Imipenem + cilastatin

Compatibility
Fluids: Glucose 5%, glucose 10%, sodium chloride 0.9%
Y-site: Aciclovir, amifostine, anidulafungin, aztreonam, caspofungin, ceftriaxone, chlorpromazine, daptomycin, flucloxacillin, ganciclovir, haloperidol lactate, metaraminol, midazolam, milrinone, mycophenolate mofetil, palonosetron, pethidine, sodium bicarbonate, vecuronium.

Incompatibility
Fluids: Hartmann’s.
Y-site: Amiodarone, amoxycillin, azathioprine, azithromycin, ceftriaxone, chlorpromazine, dapsone, fluconazole, ganciclovir, haloperidol lactate, metaraminol, midazolam, milrinone, mycophenolate mofetil, palonosetron, pethidine, sodium bicarbonate, vecuronium.

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

Storage
Vial: Store below 25°C.

Special Comments
Solutions of imipenem + cilastatin range from colourless to yellow. Variations of colour within this range do not affect the potency.

Evidence summary
Pharmacokinetics: Imipenem + cilastatin is excreted via kidneys, mainly through 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 *Pseudomonas aeruginosa*. Safety: Seizures can occur in neonates with meningitis, other CNS infections and in patients with renal impairment.

References