

## Presentation

Cispenam® 250 IV injection: Each vial contains Imipenem Monohydrate USP and Cilastatin Sodium USP equivalent to Imipenem 250 mg & Cilastatin 250 mg respectively.

Cispenam® 500 IV injection: Each vial contains Imipenem Monohydrate USP and Cilastatin Sodium USP equivalent to Imipenem 500 mg & Cilastatin 500 mg respectively.

## Description

Imipenem is an antibiotic that fights serious infections caused by bacteria. Imipenem inhibits bacterial cell wall synthesis. Cilastatin helps Imipenem work more effectively by preventing the breakdown of the antibiotic in the kidneys. Cilastatin prevents metabolism of Imipenem, resulting in increased urinary recovery and decreased renal toxicity.

## Indications and Uses

The activity of Imipenem against an unusually broad spectrum of pathogens makes it particularly useful in the treatment of polymicrobial mixed aerobic/anaerobic infections as well as initial therapy prior to the identification of the causative organisms. Cispenam is indicated for the treatment of the following infections due to susceptible organisms:

- Intra-abdominal infections
- Lower respiratory tract infections
- Gynaecological infections
- Septicaemia
- Genitourinary tract infections
- Bone and joint infections
- Skin and soft tissue infections
- Endocarditis

## Dosage and Administration

The total daily dosage of Imipenem should be based on the type or severity of infection and given in equally divided doses based on consideration of degree of susceptibility of the pathogens, renal function and body-weight.

*Cispenam IV:* Up to 500 mg dose should be given over 20 to 30 minutes; > 500 mg dose should be infused over 40 to 60 minutes. In patients who develop nausea during the infusion, the rate of infusion may be slowed.

*Adult:*  
Normal daily dose is 1-2 g administered in 3-4 divided doses. For the treatment of moderate infection, a 1 g b.i.d. dosage regimen may also be used. In infections due to less susceptible organisms, the daily dosage may be increased to a maximum of 4 g/day or 50 mg/kg/day, whichever is lower.

Mild infection: 250 mg 6 hourly (1 g/day).  
Moderate infection: 500 mg 8 hourly or 1 g 12 hourly (1.5-2 g/day).  
Severe infection with fully susceptible microorganism: 500 mg 6 hourly (2 g/day).  
Severe infection with less susceptible organisms (primarily some strains of *P. aeruginosa*): 1 g 3-4 times daily (3-4 g/day).

### Dosage adjustment in patients with impaired renal function

Normal Daily Dose	Creatinine Clearance (ml/min)		
	41-70	21-40	6-20
1.0 g/day	250 mg q8h	250 mg q12h	250 mg q12h
1.5 g/day	250 mg q6h	250 mg q8h	250 mg q12h
2.0 g/day	500 mg q8h	250 mg q6h	250 mg q12h
3.0 g/day	500 mg q6h	500 mg q8h	500 mg q12h
4.0 g/day	750 mg q8h	500 mg q6h	500 mg q12h

### Children

≥ 3 months of age: the recommended dose for non-CNS infections is 15-25 mg/kg/dose administered every six hours. The maximum daily dose for treatment of infections with fully susceptible organisms is 2 g per day, and of infections with moderately susceptible organisms is 4 g/day. Higher doses (up to 90 mg/kg/day in older children) have been used in patients with cystic fibrosis.

< 3 months of age: Following dosage schedule is recommended for non-CNS infections:

- 4 weeks-3 months. of age: 25 mg/kg every 6 hrs.
- 1-4 weeks of age: 25 mg/kg every 8 hrs
- < 1 week of age: 25 mg/kg every 12 hrs

Imipenem is not recommended for the therapy of meningitis. If meningitis is suspected, an appropriate antibiotic should be used.

Imipenem, and cilastatin are injection is not recommended in pediatric patients < 30 kg with impaired renal function, as no data are available.

### Cispenam IM injection:

Patients with lower respiratory tract infections, skin and skin structure infections, and gynecologic infections of mild to moderate severity may be treated with 500 mg or 750 mg administered every 12 hours depending on the severity of the infection.

Intra-abdominal infection may be treated with 750 mg every 12 hours.

Total daily IM dosage greater than 1500 mg per day is not recommended.

## Procedure of reconstitution

*For intravenous administration:* Vial containing 250 mg Imipenem will be reconstituted with 50 ml infusion solution and vial containing 500 mg Imipenem will be reconstituted with 100 ml infusion solution. Approximately 10 ml of the infusion solution should be added to the vial. Shake well and transfer the resulting suspension to the infusion solution container. The final concentration of imipenem will be 5 mg/ml.

*For intramuscular administration:* Cispenam 500 mg should be reconstituted with 2 ml lidocaine HCl (1% solution) and Cispenam 750 mg should be reconstituted with 3 ml lidocaine HCl (1% solution). Agitate to form a suspension, then withdraw and inject the entire contents of vial intramuscularly.

### Compatible diluents for IV solution

0.9% Sodium Chloride, 5% Dextrose in Water, 10% Dextrose in Water, 5% Dextrose & 0.9% NaCl, 5% Dextrose & 0.45% NaCl, 5% Dextrose & 0.225% NaCl, 5% Dextrose & 0.15% KCl, Mannitol 5% and 10%.

### Stability of the reconstituted solution

The stability of Cispenam IV solution is 4 hours at room temperature (25 °C) and 24 hours at 4°C.

The suspension of Cispenam IM in lidocaine HCl should be used within one hour after preparation.

## Precautions

Before therapy with Imipenem, careful inquiry should be made concerning previous hypersensitivity reactions to beta-lactam antibiotics. If an allergic reaction to Cispenam occurs, the medicine should be discontinued and appropriate measures undertaken. Antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis. It is important to consider a diagnosis of pseudomembranous colitis in patients who develop diarrhoea in association with antibiotic use.

Imipenem I.V. is chemically incompatible with lactate and should not be reconstituted in diluents containing lactate. Imipenem I.V. should not be mixed with or physically added to other antibiotics. The IV formulation is not for IM use.

## Drug Interaction

Since concomitant administration of Imipenem-Cilastatin and probenecid results in only minimal increases in plasma levels of Imipenem and plasma half-life, it is not recommended that probenecid be given with Imipenem-Cilastatin. Imipenem-Cilastatin should not be mixed with or physically added to other antibiotics. However, Imipenem may be administered concomitantly with other antibiotics, such as aminoglycosides. Case reports have shown that co-administration of carbapenems, including imipenem, to patients receiving valproic acid or divalproex sodium results in a reduction in valproic acid concentrations. The valproic acid concentrations may drop below the therapeutic range as a result of this interaction, therefore increasing the risk of breakthrough seizures. Although the mechanism of this interaction is unknown, data from in vitro and animal studies suggest that carbapenems may inhibit the hydrolysis of valproic acid's glucuronide metabolite back to valproic acid, thus decreasing the serum concentrations of valproic acid. Serum valproic acid concentrations should be monitored frequently after initiating carbapenem therapy.

## Contraindications

Hypersensitivity to any component of this product.

## Use in pregnancy & lactation

*Pregnancy:* There are no adequate and well controlled studies in pregnant women. Imipenem should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

*Lactation:* Imipenem has been detected in human milk. If the use of Imipenem is deemed essential, the patient should stop nursing.

## Adverse Effects

Imipenem is generally well tolerated. Adverse effects rarely require cessation of therapy and are generally mild and transient; serious adverse effects are rare. Adverse effects may include nausea, vomiting, diarrhoea, staining of teeth and/or tongue, taste disturbance, hearing loss, blood disorders, positive Coomb's test. Allergic reactions: Rash, pruritus, urticaria, erythema multiforme, Stevens-Johnson syndrome, angioedema, toxic epidermal necrolysis (rarely), exfoliative dermatitis (rarely), candidiasis, fever, including drug fever, anaphylactic reactions. Myoclonic activity, convulsions, confusions and mental disturbances reported, slight increase in liver enzymes and bilirubin, rarely hepatitis, increase in serum creatinine and blood urea, red coloration of urine in children.

## Overdosage

No specific information is available on the treatment of overdosage with Imipenem. Imipenem-Cilastatin Sodium is haemodialysable. However, usefulness of this procedure in the overdosage setting is unknown.

## Storage

Do not store above 30 °C. Keep away from light and out of the reach of children.

## Commercial Pack

Cispenam® 250 IV injection: Each box contains one vial containing Imipenem Monohydrate USP & Cilastatin Sodium USP equivalent to Imipenem 250 mg & Cilastatin 250 mg respectively, one bottle of 50 ml normal saline, one 10 ml sterile disposable syringe, one vial Hanger, one infusion set with butterfly needle, first aid band and alcohol pad.

Cispenam® 500 IV injection: Each box contains one vial containing Imipenem Monohydrate USP & Cilastatin Sodium USP equivalent to Imipenem 500 mg & Cilastatin 500 mg respectively, one bottle of 500 ml normal saline, one 10 ml sterile disposable syringe, one vial Hanger, one infusion set with butterfly needle, first aid band and alcohol pad.

