For the use only of Registered Medical Practitioners or a Hospital or a Laboratory

Rx Imipenem & Cilastatin for Injection IP

AMERICAN

IMSTATIN 500

Injection

(500 mg + 500 mg)

Composition:
Each vial contains :

Imipenem IP	
Eq. to Anhydrous Imipenem	500 mg
Cilastatin Sodium IP	
Eq. to Cilastatin	500 mg

(As a Sterile Mixture of Imipenem, Cilastatin Sodium & Sodium Bicarbonate)

CATEGORY
Antibacterial

PHARMACOLOGICAL INFORMATION
Mode of Action:
IMSTATIN(Imipenem & Cilastatin) is an antibiotic. Imipenem kills or stops the growth of bacteria that cause severe infections. Cilastatin is added to make imipenem work better. Imipenem-cilastatin treats many kinds of infections including those of the skin, bone, heart, blood, stomach, lungs, sinuses, and kidneys. It also treats certain infections in women (pelvic infections). Generic imipenem-cilastatin injections are not yet available.

Pharmacokinetic
Absorption & Distribution
Intravenous infusion of **IMSTATIN** over 20 minutes results in peak plasma levels of imipenem antimicrobial activity that range from 14 to 24 µg/mL for the 250 mg dose, from 21 to 58 g/mL for the 500 mg dose, and from 41 to 83 µg/mL for the 1000 mg dose. At these doses, plasma levels of imipenem antimicrobial activity decline to below 1 µg/mL or less in 4 to 6 hours.

Metabolism
Imipenem, when administered alone, is metabolized in the kidneys by dehydropeptidase It resulting in relatively low levels in urine. Cilastatin sodium, an inhibitor of this enzyme, effectively prevents renal metabolism of imipenem so that when imipenem and cilastatin sodium are given concomitantly, fully adequate antibacterial levels of imipenem are achieved in the urine.

Elimination
Urine concentrations of imipenem in excess of 10 µg/mL can be maintained for up to 8 hours with **IMSTATIN** at the 500-mg dose. Approximately 70% of the cilastatin sodium dose is recovered in the urine within 10 hours of administration of **IMSTATIN.**

Microbiology
The bactericidal activity of imipenem results from the inhibition of cell wall synthesis. Its greatest affinity is for penicillin binding proteins (PBPs) 1A, 1B, 2, 4, 5 and 6 of Escherichia coli, and 1A, 1B, 2, 4 and 5 of Pseudomonas aeruginosa. The lethal effect is related to binding to PBP 2 and PBP 1B. Imipenem has a high degree of stability in the presence of beta-lactamases, both penicillinases and cephalosporinases produced by gram-negative and gram-positive bacteria. It is a potent inhibitor of beta-lactamases from certain gram-negative bacteria which are inherently resistant to most beta-lactam antibiotics, e.g., Pseudomonas aeruginosa, Serratia spp., and Enterobacter spp

INDICATION

IMSTATIN is indicated for the treatment of serious infections caused by susceptible strains of the designated microorganisms in the conditions listed below:

A) Lower respiratory tract infections.
B) Urinary tract infections
C) Intra-abdominal infections
D) Gynecologic infections
E) Bacterial septicemia
F) Bone and joint infections
G) Skin and skin structure infections
H) Endocarditis.
I) Polymicrobic infections

CONTRAINDICATION :
IMSTATIN in patients with known hypersensitivity to any component of this product or to other drugs in the same class or in patients who have demonstrated anaphylactic reaction to beta lactams.

DRUG INTRACTIONS :
IMSTATIN should not be mixed with or physically added to other antibiotics. However, **IMSTATIN** may be administered concomitantly with other antibiotics, such as aminoglycosides.

A clinically significant reduction in serum valproic acid concentration has been reported in patients receiving carbapenem antibiotics and may result in loss of seizure control. Although the mechanism of this interaction is not fully understood, data from in vitro and animal studies suggest that carbapenem antibiotics may inhibit valproic acid glucuronide hydrolysis. Serum valproic acid concentrations should be monitored frequently after initiating carbapenem therapy. Alternative antibacterial or anticonvulsant therapy should be considered if serum valproic acid concentrations drop below the therapeutic range or a seizure occurs.

PRECAUTION :
Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients receiving therapy with β- lactams. These reactions are more likely to occur in individuals with a history of sensitivity to multiple allergens.
There have been reports of individuals with a history of penicillin hypersensitivity who have experienced severe hypersensitivity reactions when treated with another β-lactam. Before initiating therapy with **IMSTATIN** i.v., careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, other β-lactams, and other allergens. If an allergic reaction to **IMSTATIN** i.v. Occurs, discontinue the drug immediately. Serious anaphylactic reactions require immediate emergency treatment with epinephrine, oxygen, intravenous steroids, and airway management, including intubation. Other therapy may also be administered as indicated.
Seizure Potential
Seizures and other CNS adverse experiences have been reported during treatment with **IMSTATIN.**

ADVERSE REACTION :
Side effects that you should report to your prescriber or health care professional as soon as possible:
RARE OR UNCOMMON:
Difficulty breathing, wheezing, dizziness, fever or chills, sore throat, redness, blistering, peeling or loosening of the skin, including inside the mouth, seizures, severe or watery diarrhea, skin rash, itching, twitching or shaking of hands or feet.
MORE COMMON:
Headache, pain, swelling and irritation at the injection site (especially following deep shots),
Side effects that usually do not require medical attention (report to your prescriber or health care professional if they continue or are bothersome):
diarrhea, nausea, vomiting, too much saliva in the mouth.

OVERDOSAGE :
Little information is available. The LD_{50} of imipenem : cilastatin in a1:1 ratio in mice and rats is approximately 1 g/kg/day. Acute overdoses should be handled by halting therapy and treating supportively and symptomatically.

DOSAGE :
By intravenous infusion, in terms of imipenem. 1-2g daily (in 3-4 divided doses), less sensitive organisms, up to 50mg/kg daily(max. 4g daily)in 3-4 divided doses, child 3months and older, 60mg/kg (up to max. of 2g) daily in 4 divided doses, over 40kg. adult dose.
Surgical prophylaxis, 1g at induction repeated after 3hours, supplemented in high risk (e.g.–Colorectal) surgery by doses of 500mg 8 and 16 hours after induction.
Intravenous infusion, Powder for reconstitution, imipenem (as monohydrate) 500mg with cilastatin (as sodium salt) 500mg.

The dosage recommendations for **IMSTATIN** represent the quantity of imipenem to be administered. An equivalent amount of cilastatin is also present. 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 dosages greater than 1500 mg per day are not recommended.

The dosage for any particular patient should be based on the location of and severity of the infection, the susceptibility of the infecting pathogen(s), and renal function.
The duration of therapy depends upon the type and severity of the infection. Generally, **IMSTATIN** should be continued for at least two days after the signs and symptoms of infection have resolved. Safety and efficacy of treatment beyond fourteen days have not been established.

Adults With Impaired Renal FunctionThe safety and efficacy of **IMSTATIN** have not been studied in patients with creatinine clearance of less than 20 mL/min/1.73 m^2. Serum creatinine alone may not be a sufficiently accurate measure of renal function. Creatinine clearance (Ccr) may be estimated from the following equation:

$$\text{Ccr (Males)} = \frac{\text{(wt. in kg) (140 - age)}}{\text{(72) (creatinine in mg/dL)}}$$

Ccr (Females) = 0.85 x above value

Injection :
Route of Administration : For IV use only.

STORAGE : Store below 25°C. Protected from light & moisture.
Improper storage may deteriorate the product.

PRESENTATION :
Unit vial of 20 ml packed in a carton along with pack insert and Sterile Water for Injection.

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Gala No. 105 to 111, 1st Flr., Bldg. No. E-15/A,
Harihar Complex, Bhiwandi, Mumbai - 421302
E-mail: info@americanremedies.in
ICO: American Remedies LLC, DE, USA