Front

Solopime™

(C e f e p i m e) Injection

For Intravenous &
Intramuscular Use Only

سولو پائیم انجکشن

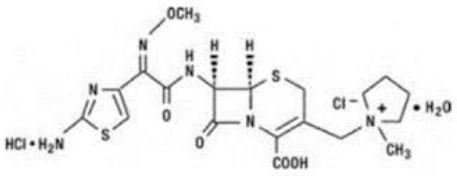
COMPOSITION:
Solopime Injection 500 mg:
Each vial contains:
Cefepime (as hydrochloride) ..... 500 mg.
(with L-Arginine)

Product Specs.: USP

Solopime Injection 1 gm:
Each vial contains:
Cefepime (as hydrochloride) ..... 1 gm.
(with L-Arginine)

Product Specs.: USP

DESCRIPTION:
Cefepime is a novel methoxyimino-aminothiazolyl cephalosporin with a quaternized N-methyl-pyrrolidine moiety at the 3' position conferring zwitterionic properties. Cefepime hydrochloride is a semi-synthetic, broad spectrum, cephalosporin antibiotic for parenteral administration. The chemical name is 1-[[(6R,7R)¬7-[2-(2-amino-4-thiazolyl)-glyoxylamido]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0] oct-2-en-3-yl]methyl]-1-methylpyrrolidinium chloride,72 -(Z)-(O-methyloxime), monohydrochloride, monohydrate, which corresponds to the following structural formula. Parenteral fourth-generation cephalosporin. Pharmacokinetics and spectrum of activity similar to ceftazidime.



CLINICAL PHARMACOLOGY:
Mechanism of Action:
Cefepime inhibits the third and final stage of bacterial cell wall synthesis by preferentially binding to specific penicillin-binding proteins (PBPs) that are located inside the bacterial cell wall. Like all beta-lactam antibiotics, cefepime's ability to interfere with PBP-mediated cell wall synthesis ultimately leads to cell lysis. Lysis is mediated by bacterial cell wall autolytic enzymes (i.e., autolysins). The relationship between PBPs and autolysins is unclear, but it is possible that the beta-lactam antibiotic interferes with an autolysin inhibitor.

Compared with third-generation cephalosporins, cefepime possesses an increased ability to penetrate the bacterial cell's outer membrane and a lower rate of hydrolysis by bacterial beta-lactamases. Cefepime exists as a zwitterion and it is thought that this property enhances its ability to penetrate porin channels in the cell walls of gram-negative bacteria. Cefepime appears to be more resistant to destruction from some beta-lactamases than are other cephalosporins. Once inside the bacterial cell, cefepime binds to penicillin-binding protein 3 (PBP-3) as other 3rd generation cephalosporins do but is unique in its ability to bind to PBP-2. The affinity for PBP-2 may explain why cefepime may be active against gram-negative bacteria that are resistant to 3rd generation cephalosporins.
Pharmacodynamics & Pharmacokinetics:
Cefepime is administered intravenously. Approximately 16% to 19% of the circulating drug is protein-bound. It is distributed into most body tissues and fluids. including human milk. Animal data suggest that cefepime penetrates into the cerebrospinal fluid (CSF) when the meninges are inflamed. The average steady-state volume of distribution of cefepime is 18 (±2) L. The serum protein binding of cefepime is approximately 20% and is independent of its concentration in serum.

Tablet 1: Average Plasma Concentrations in mcg/mL of Cefepime and Derived Pharmacokinetic Parameters (±SD). Intravenous Administration.

	CEFEPIME		
Parameter	**500 mg IV**	**1 g IV**	**2 g IV**
0.5 h	38.2	78.7	163.1
1 h	21.6	44.5	85.8
2 h	11.6	24.3	44.8
4 h	5	10.5	19.2
8 h	1.4	2.4	3.9
12 h	0.2	0.6	1.1
C_{max}, mcg/mL	39.1 (3.5)	81.7 (5.1)	163.9 (25.3)
AUC, h•mcg/mL	70.8 (6.7)	148.5 (15.1)	284.8 (30.6)
Number of subjects (male)	9	9	9

Cefepime is metabolized to N-methylpyrrolidine (NMP) which is rapidly converted to the N-oxide (NMP-N-oxide). Urinary recovery of unchanged cefepime accounts for approximately 85% of the administered dose. Less than 1% of the administered dose is recovered from urine as NMP, 6.8% as NMPN-oxide, and 2.5% as an epimer of cefepime. The elimination half-life is 2 to 2.3 hours in patients with normal renal function. Cefepime is metabolized to N-methylpyrrolidine (NMP) which is rapidly converted to the N-oxide (NMP-N-oxide). Urinary recovery of unchanged cefepime accounts for approximately 85% of the administered dose. Less than 1% of the administered dose is recovered from urine as NMP, 6.8% as NMP-N-oxide, and 2.5% as an epimer of cefepime.
Microbiology: Cefepime is a bactericidal agent that acts by inhibition of bacterial cell wall synthesis. The bacterial spectrum of cefepime includes both gram-positive and gram-negative organisms. Based on clinical reports, cefepime has equal or greater activity against Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris, Neisseria gonorrhoeae, and Providencia rettgeri than do both cefotaxime and ceftazidime. Other organisms for which cefepime has shown efficacy include Shigella, Serratia, Salmonella, and Mycobacterium species. Like other cephalosporins, cefepime is not active against enterococcus or Bacteroides. Because of this the molecule penetrates the outer cell membrane of Gram-negative bacteria rapidly. In addition, it is resistant to degradation by several plasmid and chromosomally-mediated beta-lactamases, for which it also shows very low affinity and no inducing capacity. It has good affinity for PBPs 2 and 3 of Escherichia coli and for PBP 3 of Pseudomonas aeruginosa. Its broad-spectrum of activity includes Gram-positive and Gram-negative pathogens. It is more active than cefotaxime or ceftazidime, against Enterobacteriaceae. The MIC90 for P. aeruginosa is higher than that of ceftazidime, but lower than those of cefpirome, cefoperazone and latamoxef. Other Gram-negative organisms, Haemophilus influenzae, Neiserria meningitidis, Neiserria gonorrhoeae, Moraxella catarrhalis are highly susceptible to cefepime. Among Gram-positive species methicillin-susceptible Staphylococcus aureus and coagulase-negative staphylococci, whether beta-lactamase producers or not, Streptococcus pneumoniae and Streptococcus pyogenes are susceptible.

INDICATIONS:
Cefepime is indicated in the treatment of the following infections caused by susceptible strains of the designated microorganisms.
Pneumonia (moderate to severe): Caused by Streptococcus pneumoniae, including cases associated with concurrent bacteremia, Pseudomonas aeruginosa, Klebsiella pneumoniae, or Enterobacter species
Empiric therapy for febrile neutropenic: Cefepime as monotherapy is indicated for empiric treatment of febrile neutropenic patients. In patients at high risk for severe infection (including patients with a history of recent bone marrow transplantation, with hypotension at presentation, with an underlying hematologic malignancy, or with severe or prolonged neutropenia), antimicrobial monotherapy may not be appropriate. Insufficient data exist to support the efficacy of cefepime monotherapy in such patients.
Uncomplicated and complicated urinary tract infections: (including pyelonephritis) caused by Escherichia coli or Klebsiella pneumoniae, when the infection is severe, or caused by Escherichia coli, Klebsiella pneumoniae, or Proteus mirabilis, when the infection is mild to moderate, including cases associated with concurrent bacteremia with these microorganisms.
Uncomplicated skin and skin structure infections: Caused by Staphylococcus aureus (methicillin-susceptible strains only) or Streptococcus pyogenes.
Complicated intra-abdominal infections: (used in combination with metronidazole) caused by Escherichia coli, viridans group streptococci, Pseudomonas aeruginosa, Klebsiella pneumoniae, Enterobacter species, or Bacteroides fragilis.

DOSAGE AND ADMINISTRATION:
Cefepime should be administered intravenously over approximately 30 minutes.
Empiric monotherapy of febrile neutropenia:
IV dosage in Adults: 2 g IV every 8 hours for 7 days or until resolution of neutropenia. For patients whose fever resolves the need for continued antimicrobial therapy should be reevaluated.
Infants 2 months and older, Children and adolescents: 50 mg/kg/dose IV every 8 hours (Max: 2 g/dose) for 7 days or until resolution of neutropenia. For patients whose fever resolves the need for continued antimicrobial therapy should be reevaluated.
For the treatment of complicated and uncomplicated urinary tract infection (UTI) including pyelonephritis:
IV dosage in adults: 0.5 to 1 g IV or IM every 12 hours for 7 to 10 days for mild-to-moderate infections, and 2 g IV every 12 hours for 10 days for severe infections. IM administration is only for mild-to-moderate UTIs due to E. coli when the IM route is considered a more appropriate route of administration.
Infants 2 to 11 months, Children and adolescents: 50 mg/kg/dose IV or IM every 12 hours (Max: 1 g/dose IV/IM for mild-to-moderate infections; 2 g/dose IV for severe infections). Treat for 7 to 10 days for mild-to-moderate infections and for 10 days for severe infections. IM administration is only for mild-to-moderate UTIs due to E. coli when the IM route is considered a more appropriate route of administration.
Infants 1 montht: 50 mg/kg/dose IV or IM every 12 hours.
For the treatment of complicated intraabdominal infections:
IV dosage in Adults: 2 g IV every 12 hours in combination with metronidazole for 7 to 10 days. For infections caused by Pseudomonas aeruginosa, 2 g IV every 8 hours. Guidelines suggest cefepime with metronidazole as empiric therapy in patients with high risk or severity community-acquired, health care-associated, or biliary infections.
Adolescent 17 years: 2 g IV every 12 hours in combination with metronidazole for 7 to 10 days. For infections caused by Pseudomonas aeruginosa, 2 g IV every 8 hours.
Infantst, Children†, and Adolescents 13 to 16 years: 50 mg/kg/dose IV every 12 hours (Max: 2 g/dose) in combination with metronidazole for 7 to 10 days. For infections caused by Pseudomonas aeruginosa, 50 mg/kg/dose IV every 8 hours (Max: 2 g/dose).
For the treatment of moderate to severe skin and skin structure infections due to Staphylococcus aureus or Streptococcus pyogenes or for diabetic foot ulcert:
IV dosage in Adults: 2 g IV every 12 hours for 10 days. Guidelines suggest cefepime as an empiric option in patients with moderate or severe, mixed organism diabetic foot infections in combination with agents for MRSA and anaerobes.
Infants 2 to 11 months, Children, and adolescents: 50 mg/kg/dose IV every 12 hours (Max: 2 g/dose) for 10 days.
Infants 1 montht: 50 mg/kg/dose IV every 12 hours.
For the treatment of pneumonia:
IV dosage in Adults: 2 g IV every 8 hours for at least 7 days as part of combination therapy for hospitalized patients with prior respiratory isolation of P. aeruginosa or risk factors for P. aeruginosa and recent hospitalization with parenteral antibiotic use.
Adolescents: 50 mg/kg/dose (Max: 2 g/dose) IV every 8 hours for 10 days. In HIV-infected patients, cefepime is recommended as part of combination therapy for hospitalized patients at risk for P. aeruginosa.
Powder vials for injection:
Reconstitution: Add 5 mL of compatible IV diluent to each 500 mg vial or 10 mL of diluent to each 1 g or 2 g vial. The resultant solution will be 100 mg/mL for the 500 mg and 1 g vials and 160 mg/mL for the 2 g vial. Further dilution is required. Compatible diluents include Sterile Water for Injection, 0.9% Sodium Chloride Injection, 5% Dextrose Injection, 0.5% or 1% Lidocaine Hydrochloride Injection, or Sterile Bacteriostatic Water for Injection with Parabens or Benzyl Alcohol.
Storage: Reconstituted solutions are stable for up to 24 hours at room temperature or 7 days refrigerated (2 to 8 degrees C, 36 to 46 degrees F).
Dilution: Dilute reconstituted solution with a compatible IV solution to provide a solution with a final concentration between 1 mg/mL and 40 mg/mL. Compatible solutions include 0.9% Sodium Chloride Injection, 5% Dextrose Injection, 10% Dextrose Injection, Lactated Ringer's Injection, 5% Dextrose and 0.9% Sodium Chloride Injection, Lactated Ringer's and 5% Dextrose Injection, or Normosol-R and Normosol-M in 5% Dextrose Injection.
Storage: Diluted solutions are stable for up to 24 hours at controlled room temperature or 7 days refrigerated (2 to 8 degrees C, 36 to 46 degrees F).

Back

PRECAUTIONS / CONTRAINDICATIONS:

General information: A false-positive reaction for glucose in the urine has been observed in patients receiving cephalosporins, such as cefepime, and using Benedict's solution, Fehling's solution, or Clinitest tablets for urine glucose testing. However, this reaction has not been observed with glucose oxidase tests (e.g., Tes-tape, Clinistix, Diastix). Positive direct Coombs tests have been reported during treatment with cefepime. In hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs test of newborns whose mothers received cefepime before delivery, clinicians should keep in mind that a positive Coombs test may be due to the drug.

Antimicrobial resistance, viral infection: Cefepime does not treat viral infection (e.g., common cold). Prescribing in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria (antimicrobial resistance). Patients should be told to complete the full course of treatment, even if they feel better earlier.

Cephalosporin hypersensitivity, penicillin hypersensitivity: Health care providers are advised to evaluate patients' allergy history prior to initiation of therapy. Cefepime is contraindicated in patients with cephalosporin hypersensitivity or cephamycin hypersensitivity. It should be used cautiously in patients with hypersensitivity to penicillin. Patients who have experienced severe penicillin hypersensitivity should not receive cefepime. Cross-reactivity among beta-lactam antibiotics may occur in up to 10% of patients with a documented history of penicillin hypersensitivity.

Colitis, diarrhea, GI disease, inflammatory bowel disease, pseudomembranous colitis, ulcerative colitis: Almost all antibacterial agents have been associated with pseudomembranous colitis (antibiotic-associated colitis) which may range in severity from mild to life-threatening. In the colon, overgrowth of Clostridia may exist when normal flora is altered subsequent to antibacterial administration. It is known that systemic use of antibiotics predisposes patients to development of pseudomembranous colitis. Consideration should be given to the diagnosis of pseudomembranous colitis in patients presenting with diarrhea following antibacterial administration. Systemic antibiotics should be prescribed with caution to patients with inflammatory bowel disease such as ulcerative colitis or other GI disease. If diarrhea develops during therapy, the drug should be discontinued. Following diagnosis of pseudomembranous colitis, therapeutic measures should be instituted.

Renal failure, renal impairment: Cefepime is eliminated via renal mechanisms and should be used with caution in patients with renal impairment (creatinine clearance 60 mL/min or less) or renal failure. High and prolonged serum concentrations can occur from usual dosages in patients with renal impairment or other conditions that compromise renal function, and thus the maintenance dosage should be adjusted when administered to such patients. Continued dosage should be determined by degree of renal impairment, severity of infection, and susceptibility of the causative organisms. Serious adverse events have occurred in patients with renal insufficiency given unadjusted doses of cefepime, including life-threatening or fatal encephalopathy, seizures, and/or renal failure. Health care providers are advised to discontinue therapy or make appropriate dose adjustments for any patient experiencing seizures during cefepime therapy.

Coagulopathy, vitamin K deficiency: Many cephalosporins, including cefepime, have been rarely associated with a fall in prothrombin activity (hypoprothrombinemia). Those at risk include patients with renal or hepatic impairment, or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy. Prothrombin time should be monitored in patients at risk, and exogenous vitamin K administered as indicated. Cephalosporins which contain the NMTT side chain (e.g., cefoperazone, cefamandole, cefotetan) have been particularly associated with an increased risk for bleeding. Cephalosporins should be used cautiously in patients with a preexisting coagulopathy (e.g., vitamin K deficiency) since these patients may be at a higher risk for these complications.

Special Populations:

Hepatic impairment: Specific guidelines for dosage adjustments in hepatic impairment are not available; it appears that no dosage adjustments are needed.

Renal impairment: The initial dose of cefepime for patients with renal impairment is the same as for patients with normal renal function; maintenance doses and/or dosage intervals require adjustment based on the degree of impairment.

Pediatric patients (non-neonatal): Specific data in children with impaired renal function are not available. Because cefepime pharmacokinetics are similar in adults and non-neonatal pediatric patients, changes in the dosage regimen proportional to those in adults are recommended for pediatric patients. The below recommendations for maintenance dose adjustments in pediatric patients are consistent with recommendations for adult patients with renal impairment.

For a usual dosing schedule of 50 mg/kg/dose IV every 8 hours:

- **CrCl 30 to 60 mL/minute:** 50 mg/kg/dose IV every 12 hours (Max: 2 g/dose)
- **CrCl 11 to 29 mL/minute:** 50 mg/kg/dose IV every 24 hours (Max: 2 g/dose)
- **CrCl less than 11 mL/minute:** 25 mg/kg/dose IV every 24 hours (Max: 1 g/dose)

For a usual dosing schedule of 50 mg/kg/dose IV every 12 hours:

- **CrCl 30 to 60 mL/minute:** 50 mg/kg/dose IV every 24 hours (Max: 2 g/dose)
- **CrCl 11 to 29 mL/minute:** 25 mg/kg/dose IV every 24 hours (Max: 1 g/dose)
- **CrCl less than 11 mL/minute:** 12.5 mg/kg/dose IV every 24 hours (Max: 500 mg/dose)

Pregnancy: Cefepime is classified as FDA pregnancy risk category B. Animal data reveal no teratogenic effects. There are, however, no adequate and well-controlled studies in pregnant women. Because animal studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed. Cefepime has not been studied for use during labor and delivery. Treatment should be given only if clearly needed.

Breast-feeding: Cefepime is excreted in human breast milk in very low concentrations (0.5 mcg/ml). It should be used with caution during breast-feeding and the benefits versus risks should be considered. Unless the infant is allergic to cephalosporins, breast-feeding is generally safe during maternal cephalosporin therapy; the infant should be observed for potential effects. If a breast-feeding infant experiences an adverse effect related to a maternally administered drug, healthcare providers are encouraged to report the adverse effect.

Infants, neonates: The safety and efficacy of cefepime have not been established in neonates or infants less than 2 months of age. Data support the use of cefepime in the treatment of uncomplicated and complicated urinary tract infections (including pyelonephritis), uncomplicated skin and skin structure infections, pneumonia, and as empiric therapy for febrile neutropenia in pediatric patients age 2 months to 16 years.

Geriatric: Geriatric patients are more likely to have decreased renal function; therefore, care should be taken in dose selection, and renal function should be monitored. Cefepime dosages should be adjusted if renal dysfunction is present. Overall, at the usual recommended adult dose, the clinical efficacy and safety in elderly patients were comparable to safety and efficacy in non-elderly adults.

DRUG INTERACTIONS:

Amikacin, Aminoglycosides, Gentamicin, Kanamycin, Paromomycin, Plazomicin, Streptomycin, Tobramycin: (Minor) Cefepime's product label states that cephalosporins may potentiate the adverse renal effects of nephrotoxic agents, such as aminoglycosides and loop diuretics. Carefully monitor renal function, especially during prolonged therapy or use of high aminoglycoside doses. The majority of reported cases involve the combination of aminoglycosides and cephalothin or cephaloridine, which are associated with dose-related nephrotoxicity as singular agents. Limited but conflicting data with other cephalosporins have been noted.

Loop diuretics: (Minor) Nephrotoxicity associated with cephalosporins may be potentiated by concomitant therapy with loop diuretics. Clinicians should be aware that this may occur even in patients with minor or transient renal impairment.

Oral contraceptives: (Moderate) It would be prudent to recommend alternative or additional contraception when oral contraceptives (OCs) are used in conjunction with antibiotics. It was previously thought that antibiotics may decrease the effectiveness of OCs containing estrogens due to stimulation of metabolism or a reduction in enterohepatic circulation via changes in GI flora. One retrospective study reviewed the literature to determine the effects of oral antibiotics on the pharmacokinetics of contraceptive estrogens and progestins, and also examined clinical studies in which the incidence of pregnancy with OCs and antibiotics was reported. It was concluded that the antibiotics ampicillin, ciprofloxacin, clarithromycin, doxycycline, metronidazole, ofloxacin, roxithromycin, temafloxacin, and tetracycline did not alter plasma concentrations of OCs. Anti-tuberculous drugs (e.g., rifampin) were the only agents associated with OC failure and pregnancy. Based on the study results, these authors recommended that back-up contraception may not be necessary if OCs are used reliably during oral antibiotic use. These authors concluded that because females most at risk for OC failure or noncompliance may not be easily identified and the true incidence of such events may be under-reported, and given the serious consequence of unwanted pregnancy, that recommending an additional method of contraception during short-term antibiotic use may be justified. During long-term antibiotic administration, the risk for drug interaction with OCs is less clear, but alternative or additional contraception may be advisable in selected circumstances. Data regarding progestin-only contraceptives or for newer combined contraceptive deliveries (e.g., patches, rings) are not available.

Sodium picosulfate; Magnesium oxide; Anhydrous citric acid: (Major) Prior or concomitant use of antibiotics with sodium picosulfate; magnesium oxide; anhydrous citric acid may reduce efficacy of the bowel preparation as conversion of sodium picosulfate to its active metabolite bis-(p-hydroxy-phenyl)-pyridyl-2-methane (BHPM) is mediated by colonic bacteria. If possible, avoid coadministration. Certain antibiotics (i.e., tetracyclines and quinolones) may chelate with the magnesium in sodium picosulfate; magnesium oxide; anhydrous citric acid solution. Therefore, these antibiotics should be taken at least 2 hours before and not less than 6 hours after the administration of sodium picosulfate; magnesium oxide; anhydrous citric acid solution.

Warfarin: (Moderate) The concomitant use of warfarin with many classes of antibiotics, including cephalosporins, may increase the INR thereby potentiating the risk for bleeding. Inhibition of vitamin K synthesis due to alterations in the intestinal flora may be a mechanism; however, concurrent infection is also a potential risk factor for elevated INR. Additionally, certain cephalosporins (cefotetan, cefoperazone, cefamandole) are associated with prolongation of the prothrombin time due to the methylthiotetrazole (MTT) side chain at the R2 position, which disturbs the synthesis of vitamin K-dependent clotting factors in the liver. Monitor patients for signs and symptoms of bleeding. Additionally, increased monitoring of the INR, especially during initiation and upon discontinuation of the antibiotic, may be necessary.

ADVERSE REACTIONS:

Severe: Seizures, Azotemia, Hyperkalemia, Coma, Anaphylactic Shock, Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis, Erythema Multiform, Hemolytic Anemia, Agranulocytosis, Pancytopenia, Aplastic Anemia.

Moderate: Elevated Hepatic Enzymes, Hypophosphatemia, Eosinophilia, Hypoprothrombinemia, Phlebitis, Erythema,
Candidiasis, Colitis, Vaginitis, Pseudomembranous Colitis, Anemia, Hypocalcemia, Hypercalcemia, Hyperphosphatemia, Cholestasis, Encephalopathy, Aphasia, Hallucinations, Confusion, Superinfection, Neutropenia, Bleeding, Thrombocytopenia and Leukopenia.

Mild: Rash, Injection Site Reaction, Diarrhea, Nausea, Headache, Fever, urticaria, pruritis, vomiting.

INSTRUCTIONS:

- Store in a cool and dry place, below 30ºC.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- Do not freeze.
- To be sold on the prescription of a registered medical practitioner only.

DIRECTIONS FOR RECONSTITUTION:

For 500 mg Injection:
For IM Use: Add 1.3 ml sterile water for injection in a vial.
For IV Use: Add 5 ml sterile water for injection in a vial.
For 1 gm Injection:
For IM Use: Add 2.4 ml sterile water for injection in a vial.
For IV Use: Add 10 ml sterile water for injection in a vial.

- Always use freshly reconstituted solution.
- Discard any remaining portion after administration.

PRESENTATION:

Solopime Injection 500 mg	:	Pack of 500 mg injection 1 vial + 5 ml Solvent water for injection.
Solopime Injection 1 gm	:	Pack of 1 gm injection 1 vial + 10 ml Solvent water for injection.

ہدایات:

دوا کو خشک اور ٹھنڈی جگہ، ۳۰ درجہ سینٹی گریڈ سے
کم درجہ حرارت پر رکھیں۔ گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔ منجمند ہونے سے بچائیں۔
صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

دوا تیار کرنے کا طریقہ:

۵۰۰ ملی گرام انجکشن کیلئے:
عضلاتی استعمال کیلئے: محلول بنانے کیلئے جراثیم سے پاک 1.3 ملی لیٹر پانی استعمال کریں۔
وریدی استعمال کیلئے: محلول بنانے کیلئے جراثیم سے پاک ۵ ملی لیٹر پانی استعمال کریں۔
1 گرام انجکشن کیلئے:
عضلاتی استعمال کیلئے: محلول بنانے کیلئے جراثیم سے پاک 2.4 ملی لیٹر پانی استعمال کریں۔
وریدی استعمال کیلئے: محلول بنانے کیلئے جراثیم سے پاک ۱۰ ملی لیٹر پانی استعمال کریں۔
انجکشن تیار کرنے کے فوراً بعد استعمال کریں۔
استعمال کے بعد بچ جانے والا محلول ضائع کر دیں۔

Manufactured by:
Pharmasol (Pvt.) Ltd.
Plot No. 549, Sunder Industrial Estate, Lahore, Pakistan.

FOR FURTHER INFORMATION PLEASE CONTACT:

Marketed by:
CCL Pharmaceuticals (Pvt.) Ltd.
62 Industrial Estate, Kot Lakhpat, Lahore, Pakistan.

zoom view

Front

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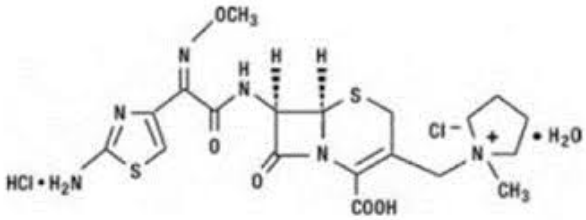

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Parameter	**500 mg IV**	**1 g IV**	**2 g IV**
0.5 h	38.2	78.7	163.1
1 h	21.6	44.5	85.8
2 h	11.6	24.3	44.8
4 h	5	10.5	19.2
8 h	1.4	2.4	3.9
12 h	0.2	0.6	1.1
C_{max}, mcg/mL	39.1 (3.5)	81.7 (5.1)	163.9 (25.3)
AUC, h•mcg/mL	70.8 (6.7)	148.5 (15.1)	284.8 (30.6)
Number of subjects (male)	9	9	9

Cefepime is metabolized to N-methylpyrrolidine (NMP) which is rapidly converted to the N-oxide (NMP-N-oxide). Urinary recovery of unchanged cefepime accounts for approximately 85% of the administered dose. Less than 1% of the administered dose is recovered from urine as NMP, 6.8% as NMPN-oxide, and 2.5% as an epimer of cefepime. The elimination half-life is 2 to 2.3 hours in patients with normal renal function. Cefepime is metabolized to N-methylpyrrolidine (NMP) which is rapidly converted to the N-oxide (NMP-N-oxide). Urinary recovery of unchanged cefepime accounts for approximately 85% of the administered dose. Less than 1% of the administered dose is recovered from urine as NMP, 6.8% as NMP-N-oxide, and 2.5% as an epimer of cefepime.
Microbiology: Cefepime is a bactericidal agent that acts by inhibition of bacterial cell wall synthesis. The bacterial spectrum of cefepime includes both gram-positive and gram-negative organisms. Based on clinical reports, cefepime has equal or greater activity against Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris, Neisseria gonorrhoeae, and Providencia rettgeri than do both cefotaxime and ceftazidime. Other organisms for which cefepime has shown efficacy include Shigella, Serratia, Salmonella, and Mycobacterium species. Like other cephalosporins, cefepime is not active against enterococcus or Bacteroides. Because of this the molecule penetrates the outer cell membrane of Gram-negative bacteria rapidly. In addition, it is resistant to degradation by several plasmid and chromosomally-mediated beta-lactamases, for which it also shows very low affinity and no inducing capacity. It has good affinity for PBPs 2

and 3 of Escherichia coli and for PBP 3 of Pseudomonas aeruginosa. Its broad-spectrum of activity includes Gram-positive and Gram-negative pathogens. It is more active than cefotaxime or ceftazidime, against Enterobacteriaceae. The MIC90 for P. aeruginosa is higher than that of ceftazidime, but lower than those of cefpirome, cefoperazone and latamoxef. Other Gram-negative organisms, Haemophilus influenzae, Neiserria meningitidis, Neiserria gonorrhoeae, Moraxella catarrhalis are highly susceptible to cefepime. Among Gram-positive species methicillin-susceptible Staphylococcus aureus and coagulase-negative staphylococci, whether beta-lactamase producers or not, Streptococcus pneumoniae and Streptococcus pyogenes are susceptible.

INDICATIONS:
Cefepime is indicated in the treatment of the following infections caused by susceptible strains of the designated microorganisms.
Pneumonia (moderate to severe): Caused by Streptococcus pneumoniae, including cases associated with concurrent bacteremia, Pseudomonas aeruginosa, Klebsiella pneumoniae, or Enterobacter species
Empiric therapy for febrile neutropenic: Cefepime as monotherapy is indicated for empiric treatment of febrile neutropenic patients. In patients at high risk for severe infection (including patients with a history of recent bone marrow transplantation, with hypotension at presentation, with an underlying hematologic malignancy, or with severe or prolonged neutropenia), antimicrobial monotherapy may not be appropriate. Insufficient data exist to support the efficacy of cefepime monotherapy in such patients.
Uncomplicated and complicated urinary tract infections: (including pyelonephritis) caused by Escherichia coli or Klebsiella pneumoniae, when the infection is severe, or caused by Escherichia coli, Klebsiella pneumoniae, or Proteus mirabilis, when the infection is mild to moderate, including cases associated with concurrent bacteremia with these microorganisms.
Uncomplicated skin and skin structure infections: Caused by Staphylococcus aureus (methicillin-susceptible strains only) or Streptococcus pyogenes.
Complicated intra-abdominal infections: (used in combination with metronidazole) caused by Escherichia coli, viridans group streptococci, Pseudomonas aeruginosa, Klebsiella pneumoniae, Enterobacter species, or Bacteroides fragilis.

DOSAGE AND ADMINISTRATION:
Cefepime should be administered intravenously over approximately 30 minutes.
Empiric monotherapy of febrile neutropenia:
IV dosage in Adults: 2 g IV every 8 hours for 7 days or until resolution of neutropenia. For patients whose fever resolves the need for continued antimicrobial therapy should be reevaluated.
Infants 2 months and older, Children and adolescents: 50 mg/kg/dose IV every 8 hours (Max: 2 g/dose) for 7 days or until resolution of neutropenia. For patients whose fever resolves the need for continued antimicrobial therapy should be reevaluated.
For the treatment of complicated and uncomplicated urinary tract infection (UTI) including pyelonephritis:
IV dosage in adults: 0.5 to 1 g IV or IM every 12 hours for 7 to 10 days for mild-to-moderate infections, and 2 g IV every 12 hours for 10 days for severe infections. IM administration is only for mild-to-moderate UTIs due to E. coli when the IM route is considered a more appropriate route of administration.
Infants 2 to 11 months, Children and adolescents: 50 mg/kg/dose IV or IM every 12 hours (Max: 1 g/dose IV/IM for mild-to-moderate infections; 2 g/dose IV for severe infections). Treat for 7 to 10 days for mild-to-moderate infections and for 10 days for severe infections. IM administration is only for mild-to-moderate UTIs due to E. coli when the IM route is considered a more appropriate route of administration.
Infants 1 montht: 50 mg/kg/dose IV or IM every 12 hours.
For the treatment of complicated intraabdominal infections:
IV dosage in Adults: 2 g IV every 12 hours in combination with metronidazole for 7 to 10 days. For infections caused by Pseudomonas aeruginosa, 2 g IV every 8 hours. Guidelines suggest cefepime with metronidazole as empiric therapy in patients with high risk or severity community-acquired, health care-associated, or biliary infections.
Adolescent 17 years: 2 g IV every 12 hours in combination with metronidazole for 7 to 10 days. For infections caused by Pseudomonas aeruginosa, 2 g IV every 8 hours.
Infantst, Childrent, and Adolescents 13 to 16 years: 50 mg/kg/dose IV every 12 hours (Max: 2 g/dose) in combination with metronidazole for 7 to 10 days. For infections caused by Pseudomonas aeruginosa, 50 mg/kg/dose IV every 8 hours (Max: 2 g/dose).
For the treatment of moderate to severe skin and skin structure infections due to Staphylococcus aureus or Streptococcus pyogenes or for diabetic foot ulcert:
IV dosage in Adults: 2 g IV every 12 hours for 10 days. Guidelines suggest cefepime as an empiric option in patients with moderate or severe, mixed organism diabetic foot infections in combination with agents for MRSA and anaerobes.
Infants 2 to 11 months, Children, and adolescents: 50 mg/kg/dose IV every 12 hours (Max: 2 g/dose) for 10 days.
Infants 1 montht: 50 mg/kg/dose IV every 12 hours.
For the treatment of pneumonia:
IV dosage in Adults: 2 g IV every 8 hours for at least 7 days as part of combination therapy for hospitalized patients with prior respiratory isolation of P. aeruginosa or risk factors for P. aeruginosa and recent hospitalization with parenteral antibiotic use.
Adolescents: 50 mg/kg/dose (Max: 2 g/dose) IV every 8 hours for 10 days. In HIV-infected patients, cefepime is recommended as part of combination therapy for hospitalized patients at risk for P. aeruginosa.
Powder vials for injection:
Reconstitution: Add 5 mL of compatible IV diluent to each 500 mg vial or 10 mL of diluent to each 1 g or 2 g vial. The resultant solution will be 100 mg/mL for the 500 mg and 1 g vials and 160 mg/mL for the 2 g vial. Further dilution is required. Compatible diluents include Sterile Water for Injection, 0.9% Sodium Chloride Injection, 5% Dextrose Injection, 0.5% or 1% Lidocaine Hydrochloride Injection, or Sterile Bacteriostatic Water for Injection with Parabens or Benzyl Alcohol.
Storage: Reconstituted solutions are stable for up to 24 hours at room temperature or 7 days refrigerated (2 to 8 degrees C, 36 to 46 degrees F).
Dilution: Dilute reconstituted solution with a compatible IV solution to provide a solution with a final concentration between 1 mg/mL and 40 mg/mL. Compatible solutions include 0.9% Sodium Chloride Injection, 5% Dextrose Injection, 10% Dextrose Injection, Lactated Ringer's Injection, 5% Dextrose and 0.9% Sodium Chloride Injection, Lactated Ringer's and 5% Dextrose Injection, or Normosol-R and Normosol-M in 5% Dextrose Injection.
Storage: Diluted solutions are stable for up to 24 hours at controlled room temperature or 7 days refrigerated (2 to 8 degrees C, 36 to 46 degrees F).

PRECAUTIONS / CONTRAINDICATIONS:

General information: A false-positive reaction for glucose in the urine has been observed in patients receiving cephalosporins, such as cefepime, and using Benedict's solution, Fehling's solution, or Clinitest tablets for urine glucose testing. However, this reaction has not been observed with glucose oxidase tests (e.g., Tes-tape, Clinistix, Diastix). Positive direct Coombs tests have been reported during treatment with cefepime. In hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs test of newborns whose mothers received cefepime before delivery, clinicians should keep in mind that a positive Coombs test may be due to the drug.

Antimicrobial resistance, viral infection: Cefepime does not treat viral infection (e.g., common cold). Prescribing in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria (antimicrobial resistance). Patients should be told to complete the full course of treatment, even if they feel better earlier.

Cephalosporin hypersensitivity, penicillin hypersensitivity: Health care providers are advised to evaluate patients' allergy history prior to initiation of therapy. Cefepime is contraindicated in patients with cephalosporin hypersensitivity or cephamycin hypersensitivity. It should be used cautiously in patients with hypersensitivity to penicillin. Patients who have experienced severe penicillin hypersensitivity should not receive cefepime. Cross-reactivity among beta-lactam antibiotics may occur in up to 10% of patients with a documented history of penicillin hypersensitivity.

Colitis, diarrhea, GI disease, inflammatory bowel disease, pseudomembranous colitis, ulcerative colitis: Almost all antibacterial agents have been associated with pseudomembranous colitis (antibiotic-associated colitis) which may range in severity from mild to life-threatening. In the colon, overgrowth of Clostridia may exist when normal flora is altered subsequent to antibacterial administration. It is known that systemic use of antibiotics predisposes patients to development of pseudomembranous colitis. Consideration should be given to the diagnosis of pseudomembranous colitis in patients presenting with diarrhea following antibacterial administration. Systemic antibiotics should be prescribed with caution to patients with inflammatory bowel disease such as ulcerative colitis or other GI disease. If diarrhea develops during therapy, the drug should be discontinued. Following diagnosis of pseudomembranous colitis, therapeutic measures should be instituted.

Renal failure, renal impairment: Cefepime is eliminated via renal mechanisms and should be used with caution in patients with renal impairment (creatinine clearance 60 mL/min or less) or renal failure. High and prolonged serum concentrations can occur from usual dosages in patients with renal impairment or other conditions that compromise renal function, and thus the maintenance dosage should be adjusted when administered to such patients. Continued dosage should be determined by degree of renal impairment, severity of infection, and susceptibility of the causative organisms. Serious adverse events have occurred in patients with renal insufficiency given unadjusted doses of cefepime, including life-threatening or fatal encephalopathy, seizures, and/or renal failure. Health care providers are advised to discontinue therapy or make appropriate dose adjustments for any patient experiencing seizures during cefepime therapy.

Coagulopathy, vitamin K deficiency: Many cephalosporins, including cefepime, have been rarely associated with a fall in prothrombin activity (hypoprothrombinemia). Those at risk include patients with renal or hepatic impairment, or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy. Prothrombin time should be monitored in patients at risk, and exogenous vitamin K administered as indicated. Cephalosporins which contain the NMTT side chain (e.g., cefoperazone, cefamandole, cefotetan) have been particularly associated with an increased risk for bleeding. Cephalosporins should be used cautiously in patients with a preexisting coagulopathy (e.g., vitamin K deficiency) since these patients may be at a higher risk for these complications.

Special Populations:

Hepatic impairment: Specific guidelines for dosage adjustments in hepatic impairment are not available; it appears that no dosage adjustments are needed.

Renal impairment: The initial dose of cefepime for patients with renal impairment is the same as for patients with normal renal function; maintenance doses and/or dosage intervals require adjustment based on the degree of impairment.

Pediatric patients (non-neonatal): Specific data in children with impaired renal function are not available. Because cefepime pharmacokinetics are similar in adults and non-neonatal pediatric patients, changes in the dosage regimen proportional to those in adults are recommended for pediatric patients. The below recommendations for maintenance dose adjustments in pediatric patients are consistent with recommendations for adult patients with renal impairment.

For a usual dosing schedule of 50 mg/kg/dose IV every 8 hours:

- **CrCl 30 to 60 mL/minute:** 50 mg/kg/dose IV every 12 hours (Max: 2 g/dose)
- **CrCl 11 to 29 mL/minute:** 50 mg/kg/dose IV every 24 hours (Max: 2 g/dose)
- **CrCl less than 11 mL/minute:** 25 mg/kg/dose IV every 24 hours (Max: 1 g/dose)

For a usual dosing schedule of 50 mg/kg/dose IV every 12 hours:

- **CrCl 30 to 60 mL/minute:** 50 mg/kg/dose IV every 24 hours (Max: 2 g/dose)
- **CrCl 11 to 29 mL/minute:** 25 mg/kg/dose IV every 24 hours (Max: 1 g/dose)
- **CrCl less than 11 mL/minute:** 12.5 mg/kg/dose IV every 24 hours (Max: 500 mg/dose)

Pregnancy: Cefepime is classified as FDA pregnancy risk category B. Animal data reveal no teratogenic effects. There are, however, no adequate and well-controlled studies in pregnant women. Because animal studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed. Cefepime has not been studied for use during labor and delivery. Treatment should be given only if clearly needed.

Breast-feeding: Cefepime is excreted in human breast milk in very low concentrations (0.5 mcg/ml). It should be used with caution during breast-feeding and the benefits versus risks should be considered. Unless the infant is allergic to cephalosporins, breast-feeding is generally safe during maternal cephalosporin therapy; the infant should be observed for potential effects. If a breast-feeding infant experiences an adverse effect related to a maternally administered drug, healthcare providers are encouraged to report the adverse effect.

Infants, neonates: The safety and efficacy of cefepime have not been established in neonates or infants less than 2 months of age. Data support the use of cefepime in the treatment of uncomplicated and complicated urinary tract infections (including pyelonephritis), uncomplicated skin and skin structure infections, pneumonia, and as empiric therapy for febrile neutropenia in pediatric patients age 2 months to 16 years.

Geriatric: Geriatric patients are more likely to have decreased renal function; therefore, care should be taken in dose selection, and renal function should be monitored. Cefepime dosages should be adjusted if renal dysfunction is present. Overall, at the usual recommended adult dose, the clinical efficacy and safety in elderly patients were comparable to safety and efficacy in non-elderly adults.

DRUG INTERACTIONS:

Amikacin, Aminoglycosides, Gentamicin, Kanamycin, Paromomycin, Plazomicin, Streptomycin, Tobramycin: (Minor) Cefepime's product label states that cephalosporins may potentiate the adverse renal effects of nephrotoxic agents, such as aminoglycosides and loop diuretics. Carefully monitor renal function, especially during prolonged therapy or use of high aminoglycoside doses. The majority of reported cases involve the combination of aminoglycosides and cephalothin or cephaloridine, which are associated with dose-related nephrotoxicity as singular agents. Limited but conflicting data with other cephalosporins have been noted.

Loop diuretics: (Minor) Nephrotoxicity associated with cephalosporins may be potentiated by concomitant therapy with loop diuretics. Clinicians should be aware that this may occur even in patients with minor or transient renal impairment.

Oral contraceptives: (Moderate) It would be prudent to recommend alternative or additional contraception when oral contraceptives (OCs) are used in conjunction with antibiotics. It was previously thought that antibiotics may decrease the effectiveness of OCs containing estrogens due to stimulation of metabolism or a reduction in enterohepatic circulation via changes in GI flora. One retrospective study reviewed the literature to determine the effects of oral antibiotics on the pharmacokinetics of contraceptive estrogens and progestins, and also examined clinical studies in which the incidence of pregnancy with OCs and antibiotics was reported. It was concluded that the antibiotics ampicillin, ciprofloxacin, clarithromycin, doxycycline, metronidazole, ofloxacin, roxithromycin, temafloxacin, and tetracycline did not alter plasma concentrations of OCs. Anti-tuberculous drugs (e.g., rifampin) were the only agents associated with OC failure and pregnancy. Based on the study results, these authors recommended that back-up contraception may not be necessary if OCs are used reliably during oral antibiotic use. These authors concluded that because females most at risk for OC failure or noncompliance may not be easily identified and the true incidence of such events may be under-reported, and given the serious consequence of unwanted pregnancy, that recommending an additional method of contraception during short-term antibiotic use may be justified. During long-term antibiotic administration, the risk for drug interaction with OCs is less clear, but alternative or additional contraception may be advisable in selected circumstances. Data regarding progestin-only contraceptives or for newer combined contraceptive deliveries (e.g., patches, rings) are not available.

Sodium picosulfate; Magnesium oxide; Anhydrous citric acid: (Major) Prior or concomitant use of antibiotics with sodium picosulfate; magnesium oxide; anhydrous citric acid may reduce efficacy of the bowel preparation as conversion of sodium picosulfate to its active metabolite bis-(p-hydroxy-phenyl)-pyridyl-2-methane (BHPM) is mediated by colonic bacteria. If possible, avoid coadministration. Certain antibiotics (i.e., tetracyclines and quinolones) may chelate with the magnesium in sodium picosulfate; magnesium oxide; anhydrous citric acid solution. Therefore, these antibiotics should be taken at least 2 hours before and not less than 6 hours after the administration of sodium picosulfate; magnesium oxide; anhydrous citric acid solution.

Warfarin: (Moderate) The concomitant use of warfarin with many classes of antibiotics, including cephalosporins, may increase the INR thereby potentiating the

risk for bleeding. Inhibition of vitamin K synthesis due to alterations in the intestinal flora may be a mechanism; however, concurrent infection is also a potential risk factor for elevated INR. Additionally, certain cephalosporins (cefotetan, cefoperazone, cefamandole) are associated with prolongation of the prothrombin time due to the methylthiotetrazole (MTT) side chain at the R2 position, which disturbs the synthesis of vitamin K-dependent clotting factors in the liver. Monitor patients for signs and symptoms of bleeding. Additionally, increased monitoring of the INR, especially during initiation and upon discontinuation of the antibiotic, may be necessary.

ADVERSE REACTIONS:
Severe: Seizures, Azotemia, Hyperkalemia, Coma, Anaphylactic Shock, Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis, Erythema Multiform, Hemolytic Anemia, Agranulocytosis, Pancytopenia, Aplastic Anemia.
Moderate: Elevated Hepatic Enzymes, Hypophosphatemia, Eosinophilia, Hypoprothrombinemia, Phlebitis, Erythema,
Candidiasis, Colitis, Vaginitis, Pseudomembranous Colitis, Anemia, Hypocalcemia, Hypercalcemia, Hyperphosphatemia, Cholestasis, Encephalopathy, Aphasia, Hallucinations, Confusion, Superinfection, Neutropenia, Bleeding, Thrombocytopenia and Leukopenia.
Mild: Rash, Injection Site Reaction, Diarrhea, Nausea, Headache, Fever, urticaria, pruritis, vomiting.

INSTRUCTIONS:
- Store in a cool and dry place, below 30ºC.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- Do not freeze.
- To be sold on the prescription of a registered medical practitioner only.

DIRECTIONS FOR RECONSTITUTION:
For 500 mg Injection:
For IM Use: Add 1.3 ml sterile water for injection in a vial.
For IV Use: Add 5 ml sterile water for injection in a vial.
For 1 gm Injection:
For IM Use: Add 2.4 ml sterile water for injection in a vial.
For IV Use: Add 10 ml sterile water for injection in a vial.
- Always use freshly reconstituted solution.
- Discard any remaining portion after administration.

PRESENTATION:

Solopime Injection 500 mg	:	Pack of 500 mg injection 1 vial + 5 ml Solvent water for injection.
Solopime Injection 1 gm	:	Pack of 1 gm injection 1 vial + 10 ml Solvent water for injection.

ہدایات:
دوا کو خشک اور ٹھنڈی جگہ، ۳۰ درجہ سینٹی گریڈ سے
کم درجہ حرارت پر رکھیں۔ گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔ منجمند ہونے سے بچائیں۔
صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

دوا تیار کرنے کا طریقہ:
۵۰۰ ملی گرام انجکشن کیلئے:
عضلاتی استعمال کیلئے: محلول بنانے کیلئے جراثیم سے پاک 1.3 ملی لیٹر پانی استعمال کریں۔
وریدی استعمال کیلئے: محلول بنانے کیلئے جراثیم سے پاک ۵ ملی لیٹر پانی استعمال کریں۔
1 گرام انجکشن کیلئے:
عضلاتی استعمال کیلئے: محلول بنانے کیلئے جراثیم سے پاک 2.4 ملی لیٹر پانی استعمال کریں۔
وریدی استعمال کیلئے: محلول بنانے کیلئے جراثیم سے پاک ۱۰ ملی لیٹر پانی استعمال کریں۔
انجکشن تیار کرنے کے فوراً بعد استعمال کریں۔
استعمال کے بعد بچ جانے والا محلول ضائع کر دیں۔

Manufactured by:
Pharmasol (Pvt.) Ltd.
Plot No. 549, Sunder Industrial Estate, Lahore, Pakistan.

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