Front **85x140 mm** **Back**

℞ For the use only of a Registered Medical Practitioner or Hospital or a Laboratory.

Cefepime & Sulbactam for Injection

Critipime®-S क्रिटिपाइम-एस 1.5 ग्रा / 3 ग्रा

1.5 g / 3 g

Composition :
Each vial contains :
Cefepime Hydrochloride (Sterile) IP
Eq. to Anhydrous Cefepime 1000 mg
(A Sterile Mixture of Cefepime Hydrochloride IP & Arginine IP)
Sulbactam Sodium (Sterile) IP
Eq. to Anhydrous Sulbactam 500 mg

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Eq. to Anhydrous Cefepime 2000 mg
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Sulbactam Sodium (Sterile) IP
Eq. to Anhydrous Sulbactam 1000 mg

DESCRIPTION

Cefepime and Sulbactam for injection is an injectable antibacterial combination product consisting of the Cefepime hydrochloride and the lactamase inhibitor Sulbactam sodium for intramuscular administration (Cefepime hydrochloride) is a semi- synthetic, broad spectrum, cephalosporin antibiotic for parenteral administration. The chemical name 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]1methylpyrrolidinium chloride, 7^2-(Z)-(o-Methyloxime), monohydrochloride, monohydrate. Sulbactam Sodium, a derivative of the penicillin nucleus, is a penicillin acid sulfone. Its Chemical name is Sodium; (2S,5R)-3,3-dimethyl-4,4,7-trioxo-4λ^6- thia-1-azabicyclo[3.2.0] heptane-2-carboxylate. The chemical formula is $C_8H_{10}NO_5S$. Na and the molecular weight is 255.22. Sulbactam, a triazolyt methyl penicillin acid sulphone, is a potent inhibitor of many Lactamases, in particular the plasmid mediated enzymes which commonly cause Resistance to penicillin and cephalosporin including third generation cephalosporins. Although Sulbactam has minimal antibacterial activity when used alone, the combined use of Cefepime with Sulbactam results in a synergistic effect that expands the spectrum of activity of Cefepime against many strains of beta-lactamase, producing bacteria.

ANTI - MICROBIAL SPECTRUM

Cefepime has an extended spectrum of activity against Gram - positive and Gram negative bacteria with greater activity against both Gram negative and Gram positive organisms than third generation agents. Cefepime is a bactericidal agent that act by inhibitor of bacterial cell wall synthesis. Cefepime has a broad spectrum of in vitro activity that encompasses a wide range of Gram positive and Gram negative bacteria. Cefepime has a low affinity for chromosomally- encoded beta- lactamases. Cefepime is highly resistant to hydrolysis by most beta lactamases and exhibits rapid Penetration into Gram Negative bacterial cell, Within bacterial cell, the molecular Targets of cefepime are the penicillin binding proteins (PBP). Emergence of drug resistance to cefepime was considered as less of problem till recently. ESBLs are capable of hydrolyzing penicillin, broad and extended spectrum cephalosporins. ESBL can be found in a variety of *Enterobacteriaceae species, Klebsiella pneumonia, K.oxytoca and Escherichia coli. Other organisms to harbour ESBL are Entrobacter spp, Salmonella spp, Morganella morganii, Proteus mirabilis, Serratia marcescens and P. Aeruginosa.* Cefepime is active against most ESBL producing organisms however susceptibility appears to decrease with increasing inoculum in vitro susceptibility tests and in - vivo experimental models. Use of cefepime alone has been associated with selection of ESBL producing organisms and outbreak of injection. Sulbactam generally acts as an irreversible inhibitor and inactivates both plasmid and chromosomally mediated beta - lactamases. The combination of cefepime with sulbactam is a useful combination for the treatment of infections due to ESBL producing organisms. Sulbactam augments and protects cefepime.

PHARMACOKINETICS:

Cefepime exhibits liner dose dependent pharmacokinetics over the dosage range 250 mg to 2 g and there is no evidence of drug accumulation following multiple doses in healthy adults with normal renal function. Cefepime is almost completely absorbed following IM administration . The single 500Mg, 1g or 2 g IM does of cefepime attains peak plasma concentrations of 13.9, 29.6 or 57.5 mcg/ml respectively. Plasma concentration is attained within 1.4-1.6 hrs. After8 hrs the average plasma concentration averaged 1.9, 4.5 or 8.7 mcg/mL respectively. Following IV infusion over 30 min of a single 500 mg, 1 g or 2g dose of cefepime peak plasma concentration of the drug averaged 31.6-39.1, 65.9-81.7 or 126-139.9 mcg/ml respectively. Following parenteral administration cefepime is widely distributed into tissues and fluids, including blister fluids bronchial mucosa, sputum bile, peritoneal fluid, appendix and gallbladder. Cefepime is distributed into CSF following peneteral administration . It is also excreted in human milk. Cefepime is approximately 20% bound to serum protiens, Plasma half life of cefepime Averaged 2-2.3 hours. Cefepime is partially metabolized in vivo to N-methyl pyrrolidone (NMP). The drug is eliminated principally unchanged in urine by glomerular filtration, 80-82% of single dose cefepime is extracted unchanged in urine. Cefepime is removed by haemodialysis and peritoneal dialysis. Sulbactam 0.5 g when inused over 30 min as a single dose, the peak serum level averages 27.1mcg/ml the half - life is 0.67 hour and its renal clearance is 268ml per min. Sulbactam is metabolised to a single metabolite which has been found to be micro biologically inactive. Sulbactam and its metabolite are eliminated primarily by renal excretion with 80% of the administered dose appearing as unchanged drug and the remainder as the single metabolite.

INDICATIONS:

Cefepime and sulbactam is used parenterally for the treatment of moderate to severe infections caused by or suspected of being caused by susceptible beta - lactamases producing bacteria when cefepime alone would be in effective. Cefepime and Sulbactam combination is used for following indications: For the treatment of uncomplicated and complicated urinary tract infection Uncomplicated skin and skin structure infections and complicated intra abdominal infection.

CONTRAINDICATIONS:

Cefepime and Sulbactam combination is contraindicated patients who are hypersensitive to the drugs of others cephalosporins and should be used with caution in patients with a history of hypersensitivity to penicillins. Use of cephalosporins should be avoided in patients who have had an immediate type (anaphylactic) hypersensitivity reaction to penicillins. If a hypersensitivity reaction occurs during cefepime and sulbactam therapy,

The drug should be discontinued and the patient treated with appropriated therapy e.g. Epinephrine, corticosteroids and maintenance of an adequate airway an oxygen as indicated.

WARNINGS:

Before therapy with cefepime and sulbactam for Injection is instituted, careful inquiry should be made to determine whether the patient has had previous immediate hypersensitivity reaction to cefepime, cephalosporins, penicillins or other drugs

PRECAUTIONS:

Precautions has to be taken in patients with renal and/or hepatic insufficiency. Dose adjustment is require in patients with renal failure with creatinine clearance<60mL/min.

PREGNANCY:

There are no adequate or controlled studies using cefepime and sulbactam in pregnant women or during labour and delivery.Treatment should only be given if clearly indicated.

DRUG INTERACTIONS:

Renal function should be monitored carefully if high doses of aminoglycosides are to be administered with cefepime and sulbactam because of the increased potential of nephrotoxicity and ototoxicity of aminoglycoside antibiotics. Nephrotoxicity has been reported following concomitant administration of other cephalosporins with potent diuretic such as furosemide.

ADVERSE EFFECTS:

Adverse effects with cefepime and sulbactam are smaller to those reported with cefepime alone and generally are transient and mild to moderate in severity.

ADVERSE EVENTS REPORTED WITH CEFEPIME ARE:

Incidence equal to greater than 1% Local reactions (3.0%), pain and/or inflammation(0.6%), rash (1.1%) incidence less than 1% but greater than 0.1%: Colitis(including pseudomembrane colitis), diarrhoea, fever, headache, nausea, oral monilasis, puritus, urticarial, vafinitis, vomiting. At the higher dose of 2g q8h, the incidence of probably related adverse laboratory changes, irrespective of relationship to therapy with cefepime, were reported incidence equal to or greater than 1% positive coombs test (without hemolysis((16.2%); decreased phosphorus (2.8%): increased ALT/SGPT (2.8%)AST/SGOT (2.4%) eosinophlis(1.7%)abnormal PTT(1.6%), PT(1.4%).Incidence less than 1% but greater than 0.1% increased alkaline phosphate, BUN, creatinine, phosphorus, potassium, total bilirubin, decreased calcium, hematocrit, neutrophils, platelets, WBC.

IMPAIRED HEPATIC FUNCTION:

No adjustment is necessary for patient with impaired hepatic function.

PAEDIATRIC PATIENTS(2MONTHS TO 12 YEARS):

The usual recommended dose for paediatrics patients is 40 to 50mg/kg dose administrated 8 to 12 hrs depending on the severity of infection. The maximum dose for paediatrics patients should not exceed recommended adult dose.

RECONSTITUTION AND ADMINISTRATION:

IV Infusion for the contents of vial should be reconstituted with suitable sterile water for injections IP provided with this pack. The appropriate dose of the drug should be added to a compatible IV solution. The resultant solutions are stable for 24 hours when stored at temperature of 20-25°C or 7 days in a refrigerator at 2 to 8° C. Solution of cefepime like those of most beta - Lactam antibiotics, should not be added to solution of ampicillin at a concentration greater than 40 mg/mL, and should not be added to metronidazole,vancomycin, gentamicin, tobramycin, netilmicin sulphate or aminophylline because of potential interaction. However, If concurrent therapy with cefepime indicates each of these antibiotics can be administrated separately. Cefepime should not be used with other drugs in a syringe &/ or infusion bottle since compatibility has not been established. Cefepime should not be added to blood or blood products &/or albumin hydrolysates.

Storage : Store at a temperature not exceeding 30° C. Protect from light & moisture.

Keep the medicine out of reach of children.

PRESENTATION: Dry Powder for Injection filled in clear glass vial packed in monocarton along with 10/20 mL ampoule of Sterile Water for Injections IP in a tray with Digital leaflet.

Marketed by:
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