Reason of Artwork: New Registration (Export)
Insert Size: L (95) x H (215) mm
Code No.: 20057973
Country: **Philippines** FRONT SIDE

BACK SIDE 100% Pantone 485 C

215 mm

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

CEFTRISONE-S 1.5g

Ceftriaxone & Sulbactam for Injection

(Combipack with Sterile Water for Injections BP)

Each combipack contains :
(a) 1 vial of Ceftriaxone & Sulbactam for Injection
Each vial contains:
Ceftriaxone Sodium USP (Sterile)
eq. to Anhydrous Ceftriaxone 1000 mg
Sulbactam Sodium USP (Sterile)
eq. to Anhydrous Sulbactam 500 mg
(b) 1 Ampoule of Sterile Water for Injections BP
Each Ampoule contains :
Sterile Water for Injections BP 10 ml

PHARMACEUTICAL FORM
Solution for Injection

THERAPEUTIC INDICATIONS
Infections caused by pathogens sensitive to Ceftriaxone Injection, e.g.
- Sepsis;
- Meningitis;
- Abdominal infections (peritonitis, infections of the biliary and gastrointestinal tracts);
- Infections of the bones, joints, soft tissue, skin and of wounds;
- Infections in patients with impaired defence mechanisms;
- Renal and urinary tract infections;
- Respiratory tract infections, particularly pneumonia, and ear, nose and throat infections.
- Genital infections, including gonorrhoea.
- Perioperative prophylaxis of infections.

DOSAGE AND ADMINISTRATION
Ceftriaxone & Sulbactam For Injection may be administered either by the intravenous route or intramuscularly.

Adults
The usual adult daily dose in terms of Ceftriaxone is 1-2 grams given once a day (or in equally divided doses twice a day) depending on the type and severity of the infection. The total daily dose should not exceed 4 grams.
Dosage regimen for Ceftriaxone-Sulbactam should be adjusted in patients with marked decrease in renal function (creatinine clearance of <30ml/min) and to compensate for reduced clearance less than 15ml/min patient should receive a maximum of 500mg of sulbactam every 12 hours(maximum dose 1 gram of sulbactam)

Paediatric patients
For treatment of Skin and Soft tissue infections the recommended total dailydose (in terms of Ceftriaxone) is 50-75mg/kg given once a day or (in equally divided doses twice a day). The total daily dose should not exceed 1 gram.
For treatment of acute bacterial otitis media: A single intramuscular dose of 50mg/kg (not to exceed 1gram) is recommended.
In treatment of Meningitis: The initial therapeutic dose in terms of Ceftriaxone should be 100 mg/kg (not to exceed 4 grams) Daily dose may be administered once a day or in equally divided doses 12 hourly. The usual duration of therapy is 7-14 days.
For treatment of serious infections other than meningitis: Recommended total daily dose in terms of Ceftriaxone is 50-75 mg/kg given in divided doses every 12 hors. The total daily dose (in terms of Ceftriaxone) should not exceed more than 2 grams.

CONTRAINDICATIONS
Ceftriaxone & Sulbactam For Injection is contraindicated in patients with known allergy to Cephalosporin group of antibiotics. Hypersensitivity to penicillin may pre-dispose the patient to the possibility of allergic cross-reactions.

SPECIAL WARNINGS AND PRECAUTIONS
- Superinfections with non-susceptible microorganisms may occur.
- Since pseudo-membranous colitis has been reported to occur with ceftriaxone, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of Ceftriaxone & Sulbactam For Injection.
- Ceftriaxone, if given at higher than standard doses, may get precipitated as its calcium salt in the gall bladder, the shadows of which seen under sonography, could be mistaken for gallstones. However, it is largely asymptomatic and the shadows disappear on discontinuation of therapy or in due course after the completion of therapy. Even in the case of symptomatic cases surgical interventions are not required, and they may be treated conservatively.
- Discontinuation of Ceftriaxone & Sulbactam For Injection treatment in symptomatic cases is at the discretion of the clinician.
- Like other cephalosporins, ceftriaxone is known to displace bilirubin from serum albumin. Hence caution needs to be exercised when considering Ceftriaxone & Sulbactam For Injection for the treatment of neonates with hyper-bilirubinemia. In order to avoid the risk of development of bilirubin encephalopathy, use of Ceftriaxone & Sulbactam For Injection is best avoided in neonates in general and prematures in particular.
- During prolonged treatment with Ceftriaxone & Sulbactam For Injection, blood profile should be checked at regular intervals.
- Dosage adjustments are not necessary in hepatic failure. However, in patients with hepatic dysfunction and significant renal malfunction, Ceftriaxone & Sulbactam For Injection doses should not exceed an equivalent of 2g/day of Ceftriaxone. Close serum monitoring is recommended.
- Extreme caution needs to be exercised in penicillin-sensitive patients. In case of serious hypersensivity reactions, SC administration of epinephrine and other emergency measures are recommended.
- The allergic reaction is the indication for the interruption of Ceftriaxone & Sulbactam For Injection therapy.
- Ceftriaxone & Sulbactam For Injection should not be administered to neonates in general, hyper bilirubinemic neonates in particular, and to premature babies.

95 mm

DRUG INTERACTIONS
- No impairment of renal function has been observed after concurrent administration of large doses of Ceftriaxone and potent diuretics.
- There is no evidence to suggest that Ceftriaxone increases renal toxicity of aminoglycosides.
- The elimination of Ceftriaxone is not altered by probenecid.
- Ceftriaxone and chloramphenicol have been shown to be antagonistic in *in vitro* studies.
- In cases of concomitant severe renal and hepatic dysfunction, the plasma concentrations of ceftriaxone should be determined at regular intervals.
- Coombs test may show false-positive results during Ceftriaxone therapy.
- Non-enzymatic urinary glucose estimation methods may give false-positive results.

PREGNANCY AND LACTATION
Pregnancy
Reproductive studies have been performed in mice and rats at doses upto 20 times the usual human dose and no evidence of embryo toxicity, fetotoxicity or teralogenicity. In primates no teralogenicity or embryogenicity was demonstrated at a dose approximately 3 times the human dose. There are however no well controlled studies in pregnant women. Because animal reproductive studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Breastfeeding
Low concentrations of Ceftriaxone are excreted in human milk. No risk to nursing infants have been reported but caution should be exercised when ceftriaxone sulbactam is administered to nursing women.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
Ceftriaxone-Sulbactam has been associated with dizziness, which may affect the ability to drive or operate machinery.

UNDESIRABLE EFFECTS
Diarrhoea, Nausea, Vomiting (less frequent), Stomatitis, Glossitis, Elevations of SGOT/SGPT, Eosinophilia, Thrombocytopenia, Leukopenia, Granulocytopenia, Hematoma, Exanthema, Allergic dermatitis, Pruritis, Urticaria, Edema, Erythema multiforme, Headache, Dizziness, Increase in serum creatinine, Mycosis of the genital tract, Oliguria, Fever.

OVERDOSAGE
Limited information is available on the acute toxicity of Ceftriaxone & Sulbactam For injection. No specific antidote is available for the treatment of overdose. Hemodialysis does not remove the drug from system effectively. Hence, the treatment for Ceftriaxone & Sulbactam For Injection overdose is essentially supportive and symptomatic.

PHARMACODYNAMIC PROPERTIES
Ceftriaxone is a cephalosporin/cephamycin beta-lactam antibiotic used in the treatment of bacterial infections caused by susceptible, usually gram-positive, organisms. Ceftriaxone has *in vitro* activity against gram-positive and gram-negative aerobic and anaerobic bacteria. Ceftriaxone works by inhibiting the mucopeptide synthesis in the bacterial cell wall. The beta-lactam moiety of Ceftriaxone binds to carboxypeptidases, endopeptidases, and transpeptidases in the bacterial cytoplasmic membrane. These enzymes are involved in cell-wall synthesis and cell division. By binding to these enzymes, Ceftriaxone results in the formation of of defective cell walls and cell death.
Sulbactam is a beta-lactamase inhibitor. This drug is given in combination with beta-lactam antibiotic to inhibit beta-lactamase an enzyme produced by bacteria that destroys the antibiotics. Sulbactam is an irreversible inhibitor of β-lactamase; it binds to the enzyme and does not allow it to degrade the antibiotic.

PHARMACOKINETIC PROPERTIES
Absorption
Following intramuscular administration, peak serum concentrations of Ceftriaxone and Sulbactam are seen between 15 minutes to 2 hrs. The area under curve (AUC) after IM administration is equivalent to that after IV administration of an equivalent dose, indicating 100% bioavailability of intramuscularly administered Ceftriaxone sodium. On intravenous administration Ceftriaxone sodium diffuses into the tissue fluid where if given in the recommended doses bactericidal concentrations are maintained for upto 24 hrs. Ceftriaxone is highly bound to human serum protein by about 83-90%.

Distribution
The volume of distribution of Ceftriaxone sodium is 7-12 L and that of Sulbactam is 18-27.6 L. Ceftriaxone sodium penetrates well into the extravascular spaces, tissue fluid and the synovial fluid of inflamed joints. Ceftriaxone crosses placenta and is distributed in the amniotic fluid. It is also distributed in the milk.

Metabolism
Ceftriaxone is not metabolised in the body and is eliminated uncharged via two pathways: urine and bile. Metabolism of sulbactam is less than 25%.

Excretion
40-50% of parenterally administered dose is excreted into the urine within 48 hours as active drug. Thus, high concentrations are attained in urine, whatever is not excreted via kidney is excreted through bile. 70-80% of Sulbactam is excreted by the kidney biliary excretion is minimal and renal excretion is blocked by probenecid. Sulbactam and Ceftriaxone can be removed by hemodialysis.

SHELF LIFE
24 months

STORAGE CONDITIONS
Store below 30°C. Protect from light & moisture. Do not freeze.
Keep out of reach of children

PRESENTATION
Ceftrisone-S 1.5g is available in vial

Manufactured by:
Akums Drugs & Pharmaceuticals Ltd.
2,3,4 & 5, Sector-6B, I.I.E., SIDCUL,
Ranipur, Haridwar-249 403, INDIA.

Exported by
Unosource Pharma Ltd.
India

95 mm