1. NAME OF THE MEDICINAL PRODUCT

Name: Ceftriaxone sodium and sulbactam sodium for injection

Strength: 1.5g

Pharmaceutical form: Powder for injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains Ceftriaxone Sodium equal to ceftriaxone 1g, Sulbactam Sodium equal to Sulbactam 0.5g.

3. PHARMACEUTICAL FORM

Powder for injection

White or almost white powder.

4. Clinical particulars

4.1 Therapeutic indications

Treatment of skin and soft tissue infections, cholecystitis, osteomyelitis, chronic suppurative bacterial otitis media, gonorrhoea, chancroid, syphilis, UTI infections meningitis, nosocomial infection caused by susceptible bacteria.

Cefriaxone is a broad-spectrum bactericidal antibiotic for infections of the respiratory tract especially pneumonia and ENT infections, genital infections especially gonorrhoea; renal and urinary tract infections, pre-and post-operative prophylaxis and treatment of infection; meningitis. Sulbactam is able to inhibit the most common forms of beta-lactamase but is not able to interact with the ampC cephalosporinase. Thus, it confers little protection against bacteria such as Pseudomonas geruginosa, Citrobacter, Enterobacter, and Serratia, which often express this gene.

4.2 Posology and method of administration

Adults: 1-2gm once daily or equally divided doses twice a day. Max. Daily dose 4gm.

Paediatric: For skin and soft tissue infections 50-75mg/kg once daily or equally divided doses twice a day. Max.1gm

Acute bacterial otitis media 50mg/kg I.V. Max.1gm

Meningitis 100mg/kg. Max. 4gm once daily or twice a day in equally divided doses.

Direction for use: Ceftriaxone sodium and sulbactam sodium for injection 1500mg:

For IM use: Dissolve in 5ml of water for injection.

For IV use: Dissolve in 10ml of water for injection.

4.3 Contraindications

Known allergy to ceftriaxone, other cephalosporins, Penicillins or sulbactam. Ceftriaxone is highly bound to plasma proteins and may displace bilirubin from serum albumin (avoid in neonates with jaundice). Ceftriaxone is instituted, carefully inquiry should be made to determine whether the patients has had previous hypersensitivity reactions to Cepha-losporins, Penicillins or other drugs this product should be given cautiously to penicillin-sensitivity patients. Antibiotics should be administered with caution to any

patients who has demonstrated some form of Allergy, particularly to drugs serious acute hypersensitivity reactions may require the use of subcutaneous epinephrine and other emergency measures.

4.4 Special warnings and precautions for use

Ceftriaxone sodium and sulbactam sodium for injection is excreted via both biliary and renal excretion, therefore, patients with renal failure normally require no adjustment in dosage when usual doses of Ceftriaxone are administered, but concentrations of drug in the serum should be monitored periodically if evidence of accumulation exists, dosage should be decreased accordingly.

Dosage adjustments should not be necessary in patients with hepatic dysfunction; however, in patients with both hepatic dysfunction and significant renal disease. Prolonged use of Ceftriaxone sodium and sulbactam sodium for injection may result in overgrowth of non-susceptible organisms. Careful observation of the

patients is essential, if super-infection occurs during therapy, appropriate measures should taken.Ceftriaxone sodium and sulbactam sodium for injection should be prescribed with caution in individuals with a history of gastrointestinal disease, especially colitis. Nursing Mothers: Low concentrations of Ceftriaxone are excreted in human milk. Caution should be exercised when Ceftriaxone is administrated to a nursing woman.

Pregnancy: Teratogenic Effects: Pregnancy Category B. Reproductive studies have been performed in mice and rats at doses up to 20 times the usual human dose and have no evidence of embryotoxicity, fetotoxicity or teratogenicity. In primates, no embryotoxicity or teratogenicity was demonstrated at a dose approximately 3 times the human dose.

There are, however, no adequate and 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.

4.5 Interaction with other medicinal products and other forms of interaction

Ceftriaxone has an N-methylthiotriazine side-chain and may have the potential to increase the effects of anticoagulants and to cause a disulfiram like reaction with alcohol, as may cephalosporins with the related. N-methylthiotetrazole side chain.

4.6 Pregnancy and Lactation

Pregnancy: Teratogenic Effects: Pregnancy Category B. Reproductive studies have been performed in mice and rats at doses up to 20 times the usual human dose and have no evidence of embryotoxicity, fetotoxicity or teratogenicity. In primates, no embryotoxicity or teratogenicity was demonstrated at a dose approximately 3 times the human dose.

There are, however, no adequate and 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.

Nursing Mothers: Low concentrations of Ceftriaxone are excreted in human milk. Caution should be exercised when Ceftriaxone is administrated to a nursing woman.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Ceftriaxone sodium and sulbactam sodium for injection is generally well tolerated. The following adverse reactions were observed: local reactions (pain) , hypersensitivity (rash, pruritus, fever or chills), gastrointestinal (diarrhea, nausea), rarely headache, dizziness, vaginitis, abdominal pain.

4.9 Overdose

Ultrasonographic shadows suggesting precipitations in the kidneys accompanied by calcium ceftriaxone precipitate in the urine was observed in 1 patient dosed at 10 g/day (2.5 times the maximum recommended dose). No other case of over dosage has been reported to date. No specific information on symptoms or treatment is available. Excessive serum concentration of ceftriaxone cannot be reduced by hemodialysis or peritoneal dialysis. Treatment should be symptomatic.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Ceftriaxone is a bactericidal cephalosporin that inhibits bacterial cell wall synthesis. It is very stable in the presence of beta-lactamases, produced by Gram-positive and Gram - negative bacteria. In vitro studies indicate that the bactericidal action of ceftriaxone results from the inhibition of cell-wall synthesis. In E. coli, ceftriaxone showed a high affinity for penicillin binding proteins (PBP) la and 3 and a moderate affinity for lb and 2. In H influenza, the highest affinity was shown for PBP 4 and PBP 5. The binding affinity to PBP 4 was 35 fold that of PBP 3, ten fold that of PBP 2 and approximately 100 fold that of PBP 1. The morphological changes resulting from the PBP binding include filament formation or cell wall and septal thickening, and then cell lysis. A wide range of beta-lactamases found in microorganisms resistant to penicillins and cephalosporins have been shown in biochemical studies with cell free bacterial systems to be irreversibly inhibited by sulbactam. In particular, sulbactam has good inhibitory activity against the clinically important plasmid mediated beta-lactamases most frequently responsible for transferred drug resistance.

The presence of sulbactam in Ceftriaxone sodium and sulbactam sodium for injection Injection (ceftriaxone and sulbactam) formulation effctively extends the antibiotic spectrum of ceftriaxone to include many bacteria normally resistant to it and to other beta-lactam antibiotics. Thus, Ceftriaxone sodium and sulbactam sodium for injection possesses the properties of a broad-spectrum antibiotic and a beta-lactamase inhibitor.

5.2 Pharmacokinetic properties

Ceftriaxone is completely absorbed with peak plasma concentrations of 40mcg/ml and 80mcg/ml at 2 to 3

hours after IM injection of 500mg and 1g dose of Ceftriaxone respectively. It follows a dose dependent non-linear pharmacokinetic because of the high (80-85%) plasma protein. A similar AUC is observed after administration of an equivalent dose of Ceftriaxone by the IM or IV route. Widely distributed in body tissues and fluid, it crosses the inflamed as well as non-inflamed meninges and may achieve therapeutic concentrations in the CSF.

Irrespective of the dose Ceftriaxone has a half-life of between 6 to 9 hours. The half-life may be prolonged in neonates. While moderate renal impairment may not affect the half-life of Ceftriaxone appreciably, severe renal impairment does, with a longer half-life, which is further increased if accompanied with liver impairment. Ceftriaxone at 1 - 2 g dose achieves concentrations above the MICS in the lung, heart, biliary tract/liver, tonsil, middle ear and nasal mucosa, bone; and cerebral, pleural, prostatic and synovial fluids for most of the pathogens responsible for infection, even after more than 24 hours.

Urinary excretion by glomerular filtration accounts for 50-60% of the elimination. The intestinal flora has been shown to convert ceftriaxone into inactive metabolites. Biliary route accounts for 40-50% of excretion. In case of renal impairment the biliary excretion may be the major pathway for excretion.

In Infants & Children: Elimination half-life in neonates is prolonged which decreases with increasing postnatal age. In infants aged less than 8 days and in elderly persons aged over 75 years, the average elimination half-life is usually 2 - 3 times that seen in the adults.

In patients with renal failure, non-renal elimination may compensate.

Sulbactam has a half-life of about 1 hour in healthy volunteers. Serum concentrations reached are proportional to the dose administered. It is predominantly eliminated through kidney in the unchanged form.

5.3 Preclinical safety data

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Not applicable

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and contents of container <and special equipment for use, administration or

implantation>

Ceftriaxone sodium and sulbactam sodium for injection 1.5g/vial is available in 12ml glass vial, sealed with rubber stopper and capped with compound aluminium-plastic cap.

6.6 Special precautions for disposal <and other handling>

Any unused medicinal product or waste material should be disposed in accordance with local requirements.

7. <APPLICANT/MANUFACTURER>

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