Ceftriaxone and Sulbactam for Injection with Sterile Water for Injection BP10ml

1.3.1 SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. (Invented) Name of the medicinal product: Ceftriaxone and Sulbactam for Injection with Sterile Water for Injection BP10ml)
Strength: 1000 + 500 mg

2. Qualitative and quantitative composition:
Each combipack contains:

1. One vial of Ceftriaxone & Sulbactam for Injection

Each Vial contains:

Sterile Ceftriaxone Sodium USP

Eq. to Anhydrous Ceftriaxone..... 1000 mg

Sterile Sulbactam Sodium USP

Eq. to Anhydrous Sulbactam.....500 mg

2. One Ampoule of Sterile Water for Injection BP

Each ampoule contains:

Sterile water for Injection BP……..10ml

3. Pharmaceutical Form: Powder for Injection
Description: White or yellowish or white to off white crystalline powder filled in clear glass vials, sealed with grey butyl rubber plug and flip off aluminium seal.

4. Clinical Particulars
4.1 Therapeutic indications:
Ceftriaxone & Sulbactam for Injection is indicated in infections caused by Ceftriaxone sodium-sensitive pathogens and may be used in the clinical settings in Sepsis, Meningitis, Abdominal Infections (e.g. Peritonitis, infection of the biliary tract), infections of the Bones, Joints, Soft tissue, Skin and of wounds, Renal and Urinary Tract Infections, Respiratory tract Infections, particularly Pneumonia, and Ear, Nose and Throat Infections, and uncomplicated gonorrhea. Ceftriaxone & Sulbactam for Injection may also be used for Peri-operative Prophylaxis of Infections. A single dose given Preoperatively may reduce chances of Postoperative Infection.

4.2 Posology and method of administration:
Adults:
Usual Recommended Dose: 1.5 g to 3 g of Injection (1 g / 2 g ceftriaxone + 0.5 g / 1 g sulbactam) per day given once a day or in two equally divided doses every 12 hours. The total

daily dose of ceftriaxone should not exceed 4 grams. Also, the total dose of sulbactam should not exceed 4 grams per day.

For Uncomplicated Gonococcal Infections: A single dose of 750 mg Injection (500 mg ceftriaxone + 250 mg sulbactam) to be administered by I.M. route.

For Preoperative Use (Surgical Prophylaxis): A single dose of 1.5 g Injection (1g ceftriaxone + 0.5 g sulbactam) to be administered intravenously 30 minutes to 2 hours before surgery. The usual duration of therapy is 4 to 14 days. In complicated infections, longer therapy may be required. Or, as prescribed by the physician.

Pediatric Patients: 50 to 75 mg/kg/day, given in divided doses every 12 hours. The total daily dose of ceftriaxone should not exceed 2 grams. Sulbactam dose in children should not exceed 100 mg/kg/day.

Method of administration: I.M./I.V. Use

4.3 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.

4.4 Special warnings and precautions for use:

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 hypersensitivity 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, hyperbilirubinemic neonates in particular, and to premature babies.

4.5 Interaction with other medicinal products and other forms of interactions:

Ceftriaxone

Amsacrine, Vancomycin, Fluconazole, and Aminoglycosides: Ceftriaxone is incompatible with these drugs.

Oral Contraceptives: Ceftriaxone may adversely affect the efficacy of oral hormonal contraceptives. Consequently, it is advisable to use supplementary (non-hormonal) contraceptive measures during treatment and in the month following treatment.

Chloramphenicol: Caution is advised if concurrent administration of ceftriaxone with chloramphenicol is proposed.

Vitamin K Antagonist: Concomitant use of ceftriaxone with vitamin K antagonists may increase the risk of bleeding. Coagulation parameters should be monitored frequently, and the dose of the anticoagulant adjusted accordingly, both during and after treatment with ceftriaxone.

Sulbactam:

Probenecid: Probenecid decreases the renal tubular secretion of sulbactam. Concurrent use of probenecid with sulbactam may result in increased and prolonged blood levels of sulbactam.

4.6 Pregnancy and lactation:

Reproductive studies on ceftriaxone have been performed in mice and rats at very high doses. No evidence of embryotoxicity, fetotoxicity or teratogenicity was observed. However, in absence of adequate and well- controlled studies in pregnant women, and since reproductive animal studies may not always reflect human response, this drug should be used during pregnancy only if clearly needed. As ceftriaxone is secreted in the breast-milk, albeit at low concentrations, caution should be exercised in nursing mothers.

4.7 Effects on ability to drive and use machines:

None stated.

4.8 Undesirable effects:

Gastrointestinal: Pancreatitis, stomatitis, glossitis. Genitourinary: Oliguria, ureteric obstruction, post-renal acute renal failure. Dermatologic: Exanthema, allergic dermatitis, urticaria, edema; acute generalized exanthematous pustulosis (AGEP) and isolated cases of severe cutaneous adverse reactions (erythema multiforme, Stevens-Johnson syndrome or Lyell's syndrome / toxic epidermal necrolysis) have been reported. Hematological: Isolated cases of agranulocytosis have been reported, most of them after 10 days of treatment and following total doses of 20 g or more. Nervous System Disorders: Convulsion. Others: Symptomatic precipitation of ceftriaxone-calcium salt in the gallbladder, kernicterus, oliguria, and anaphylactic or anaphylactoid reactions. Cephalosporin Class Adverse Reactions: Allergic reactions, drug fever, serum sickness-like reaction, renal dysfunction, toxic nephropathy,

reversible hyperactivity, hypertonia, hepatic dysfunction including cholestasis, aplastic anemia, hemorrhage, fixed drug eruption (FDE) and superinfection.

4.9 Overdose:

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.

5. Pharmacological Properties:

5.1 Pharmacodynamics Properties

Pharmacotherapeutic group: Combinations of Cephalosporin and beta-lactamase inhibitors;
Mechanism of action

Ceftriaxone is a third generation cephalosporin class of beta-lactam antibiotic. Ceftriaxone inhibits bacterial cell wall synthesis and produces bactericidal effect. Ceftriaxone has activity in the presence of some beta-lactamases, both penicillinases and cephalosporinases, of Gram-negative and Gram-positive bacteria

Beta-lactamases are the enzymes produced by certain bacteria to develop resistant to penicillin and cephalosporin class of beta-lactam antibiotics. Sulbactam inhibits action of these enzymes irreversibly. In particular, sulbactam has good inhibitory activity against the clinically important plasmid mediated beta-lactamases most frequently responsible for transferred drug resistance. The addition of sulbactam effectively extends the antibacterial spectrum of concurrently administered beta-lactam antibiotic (e.g., ceftriaxone) to include many bacteria normally resistant to it.

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 halflife 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 halflife 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:
None Known

6. Pharmaceutical particulars:
6.1 List of Excipients
None

6.2 Incompatibilities
No impairment of renal function has been observed after concurrent administration of large doses of Ceftriaxone and potent diurectics. 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.

6.3 Shelf life: 24 Months

6.4 Special precautions for storage
Store in a cool & dry place below 30°C.

6.5 Nature and contents of container
1 glass vial packed in a unit carton with pack insert in combipack with 10 ml ampoule of Sterile Water for Injection BP.

6.6 Special precautions for disposal and handling
None

7. Marketing authorization holder and Manufacturing addresses:
MA Holder
BARI PHARMACY NIG. LTD.

Ceftriaxone and Sulbactam for Injection with Sterile Water for Injection BP10ml

Manufacturer

SHAMSHREE LIFESCIENCE LTD.

Plot No. 11, Industrial Area, Katha-Bhatolikalan,

Baddi 173205 (H.P.)

India