1. NAME OF THE MEDICINAL PRODUCT

Trade Name: BACTROSTAR

INN: Ceftriaxone for injection USP

Route of Administration: Intramuscular and Intravenous

2. QUALITY AND QUANTITATIVE COMPOSITION:

No	Component	Label Claim	Function	Pharmacopieal reference
1	Ceftriaxone Sodium equivalent to Ceftriaxone	1000 mg	Antibacterial	USP

3. PHARMACEUTICAL FORM:

Powder for injection

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS:

- Lower respiratory tract infections
- Acute Bacterial Otitis Media
- Skin and Skin structure infections
- Urinary tract infections (Complicated and uncomplicated)
- Pelvic inflammatory Diseases.
- Bacterial Septicemia
- Bone and Joint infections
- Meningitis
- Sexually transmitted diseases.
- Surgical prophylaxis
- The pre operative administration of Ceftriaxone may reduce the incidence of postoperative infections in patients undergoing surgical procedures.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION:

Adults & children over twelve: (Dose in terms of Ceftriaxone) is Ceftriaxone may be administered by deep intramuscular injection or as a slow intravenous injection after reconstitution of the solution according to the directions given below. The dosage and mode of administration should be determined by the severity of the infection, susceptibility of the causative organism and the patient's condition.
Intramuscular injection: 1g Ceftriaxone should be dissolved in 3.5ml of 1% Lignocaine Hydrochloride Injection BP or 3.6 ml of Sterile Water for Injections BP. The solution should be administered by deep intramuscular injection. Doses greater than 1g should be divided and injected at more than one site.
Intravenous injection: 1g Ceftriaxone should be dissolved in 9.6 ml of Sterile Water for Injections BP. The injection should be administered over at least 2-4 minutes, directly into the vein or via the tubing of an intravenous infusion. Or as directed by the Physician.

Paediatric patients
For treatment of Skin and Soft tissue infections the recommended total daily dose (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 50 mg/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 hrs.
The total daily dose (in terms of Ceftriaxone) should not exceed more than 2 grams.

Generally BACTROSTAR therepy should be continued for at least2 days after the signs and symptoms of infection have disappeared. The usual duration of therapy is 4 to 14 days,in complicated infections, longer therepy may be required

Administration:
BACTROSTAR may be administered intravenously or intramuscularly after reconstitution with sterile water for injection.
It is advisable to use the re constituted solution (as per above dilution) immediately.

4.3 CONTRAINDICATIONS:

The use of it is contraindicated in individuals with a history of hypersensitivity reactions to any of the penicillins and to the cephalosporin class of antibiotics.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE:

SPECIAL WARNING
Serious or occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients receiving beta-lactum therapy. These reactions are more likely to occure in individuals with a history of hypersensitivity reactions to multiple allergens. If an allergic reaction develops , the drug should be discontinued and appropriate therapy instituted. Pseudomembranous colitis has been reported with the use of cephalosporins[and other broad-spectrum antibiotics];therefore it is important to consider its diagnosis in patients who develop diarrhea in association with antibiotic use.
Treatment with broad spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate a toxin produced by Clostridum difficile is the primary cause of antibiotic associated colitis. Mild cases of colitis may respond to drug discontinuance alone.
Moderate to severe cases should be managed with fluid, electrolyte, and protein supplementation as indicated.

PRECAUTIONS:
General:
Although transisent elevations of BUN and serum creatinine have been observed, at the recommended dosages, the nephrotoxic potential of Ceftriaxone is similar to that of other Cephalosporins.
Ceftriaxone is excreted via both billary and renal excretion. Therefore , patients with renal failure normally require no adjustment in dosage when usual doses of Ceftriaxone are administrated but concentration of drug in the serum should be monitored periodically. If evidence of accumulation exists, dosage should be decreased accordingly.
Dosage adjustment should not be necessary in patients with hepatic dysfunction;however in patients with both hepatic dysfunction and significant renal diseases, dosage should not exceed 2gm. daily without close monitoring of serum concentrations.
Alterations in prothrombin time have occurred rarely in patients treated with Ceftriaxone. Patients with impaired vitamin K synthesis or low vitamin K stores[e.g. chronic diseases and malnutrition]

may require monitoring of protrombin time during ceftriaxone treatment.Vitamin K administration (10 mg week) may be necessary if the prothrombin time is prolonged before or during therepy.
BACTROSTAR should be prescribed with caution in individuals with a history of gastrointestinal disease, especially colitis.
If any foreign matter is visible in the vial after dissolving the contents, please do not use the solution.
Prolonged use of BACTROSTAR may result in overgrowth of non susceptible organisms. Careful observation of the patient is essential. If super infection occurs during therapy appropriate measure should be taken.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTIONS:

No impairment of renal function has been observed after concurrent administration of large doses of Ceftriaxone and potent diuretics (e.g. Furosemide). There is no evidence that ceftriaxone increases renal toxicity of aminoglycosides. No effect similar to that of disulfiram has been demonstrated after administration of alcohol with Ceftriaxone. Ceftriaxone does not contain an N-methylthiotetrazole moeity associated with possible ethanol intolerance and bleeding problems.
The elimination of Ceftriaxone is not altered by probenecid. In an in vitro-study antagonistic effects have been observed with the combination of Chloramphenicol & Ceftriaxone.
In patients treated with Ceftriaxone the Coombs test may become false positive . Ceftriaxone, like other antibiotics , may result in false – positive tests for galactosemia.
Likewise , non enzymatic methods for the glucose determination in urine may give false – positive results. For this reason, urine – glucose determination during therapy with Ceftriaxone should be done enzymatically.

4.6 PREGNANCY AND LACTATION:

Teratogenic effects:
Pregnancy category B. Reproductive studies have been performed in mice and rats , at a dose up to 20times the usual human dose and have no evidence of embryotoxicity, fatotoxicity and teratogenecity to primates , no embryotoxicity or teratogenecity was remonstrated at a dose approximately 3 times a human dose.

Nonteratogenic effects
In rats in the segment I (fertility and general reproduction) and segment III (perinatal and postnatal) studies with intravenously administered Ceftraixone, no adverse effects were noted on various reproductive parameters during gestation and lactation, including post natal growth , functional behavior and reproductive ability of the offspring, at doses of 586 mg/kg/day or less.
There are, however, no adequate and well controlled studies in pregnant women. Because animal reproductive studies are not always predictive of human response, these drugs should be used during pregnancy only if clearly needed.

Nursing mothers
Low concentration of Ceftriaxone are excreted in human milk, No risk to nursing infants has been reported but caution should be exercised when Ceftriaxone is administrated to a nursing women.
Safety in human pregnancy has not been established.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:

No studies on the effects on the ability to drive and use machines have been performed.

4.8 SIDE EFFECTS:

BACTROSTAR generally well tolerate
Local reactions: Pain, induration and tendemess at site of injection, phlebitis.
Hypersensitivity: Less frequently reported were rash, pruritus, fever or chills

Hematologic: Eosinophilia, thrombocytosis and leucopenia
Gastrointestinal: Diarrhoea, Nausea, vomiting
Hepatic: elevations of AST or ALT
Less frequently reported were elevations of alkaline phosphatase and bilirubin.
Renal: elevations of BUN
CNS: headache or dizziness were reported occasionally.
GENITOURINARY moniliasis or vaginitis were reported occasionally.
MISCELLANEOUS sdiaphoresis and flushing were reported occasionally.
Other rarely observed adverse reactions (<0.1%) include abdominal pain, agranulocytosis, allergic pneumonitis, anaphylaxis, basophilia, biliary lithiasis,
Bronchospasm, colitis, dyspepsia, epistaxis, flatulence, gallbladder sludge, glycosuria.
Other rare adverse reactions include, hematuria, jaundice, leukocytosis,lymphocytosis, monocytosis, nephrolithiasis, palpitations, a decrease in the prothrombin time, renal precipitations, seizures, and serum sickness.

4.9 OVERDOSE:

In the case of overdosage, plasma concentrations would not be reduced by haemodialysis or peritoneal dialysis. There is no specific antidote. Treatment of overdosage should be symptomatic.

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Ceftriaxone has potent bactericidal activity against a wide range of Gram-positive and, especially, Gram-negative organisms. The spectrum of activity includes both aerobic and some anaerobic species. It has considerable resistance to degradation by most bacterial β-lactamases.
Ceftriaxone kills bacteria by interfering with the synthesis of the bacterial cell wall. Ceftriaxone binds with high affinity to penicillin binding proteins in the bacterial cell wall, thus interfering with peptidoglycan synthesis. The final stage in the synthesis or peptidoglycan involves the completion of the cross-linking, and the terminal glycine residue of the pentaglycine bridge is linked to the fourth residue of the pentapeptide (D-alanine). The transpeptidase enzyme that performs this step is inhibited by cephalosporins and penicillins. As a result the bacterial cell wall is weakened, and the cell swells and then ruptures.

5.2 PHARMACOKINETIC PROPERTIES:

The pharmacokinetics of Ceftriaxone are largely determined by its concentration-dependent binding to plasma albumin. Plasma concentrations: Mean peak concentrations after bolus intravenous injection are about 120mg/l following a 500mg dose and about 200mg/l following a 1g dose; mean levels of 250mg/l are achieved after infusion of 2g over 30 minutes. Intramuscular injection of 500mg Ceftriaxone in 1% lignocaine produces mean peak plasma concentrations of 40-70 mg/l within one hour. Bioavailability after intramuscular injection is 100%.
Excretion: Ceftriaxone is eliminated mainly as unchanged drug, approximately 60% of the dose being excreted in the urine (almost exclusively by glomerular filtration) and the remainder via the biliary and intestinal tracts. The total plasma clearance is 10-22 ml/min. The renal clearance is 5-12 ml/min. A notable feature of Ceftriaxone is its relatively long plasma elimination half-life of approximately eight hours which makes single or once daily dosage of the drug appropriate for most patients. The half-life is not significantly affected by the dose, the route of administration or by repeated administration.

5.3 PRECLINICAL SAFETY DATA:

Carcinogenesis
Considering the maximum duration of treatment and the class of the compound,carcinogenic studies with Ceftriaxone in animals have not been performed. The maximum duration of animal toxicity studies was 6 months.

Mutagenesis
Genetic toxicological tests included the Ames test, a micronucleus test and a test for chromosomal aberrations in human lymphocytes cultured in vitro with Ceftriaxone. Ceftriaxone showed no potential mutagenic activity in these studies

Impairment of fertility
Ceftriaxone produced no impairment in fertility when given intravenously to rats at daily doses upto 586 mg/kg/day, approximately 20 times the recommended dose of 2 gm/day.

6. PHARMACEUTICAL PARTICULARS:

6.1 LIST OF EXCIPIENTS:
No Excipients are used.

6.2 INCOMPATIBILITIES:
Not applicable.

6.3 SHELF-LIFE:

Unopened: 24 months
After reconstitution: The reconstituted solution should be used within one hour.

6.4 SPECIAL PRECAUTIONS FOR STORAGE:
This medicinal product does not require any special storage conditions.
Do not freeze the reconstituted solution.

6.5 NATURE AND CONTENT OF CONTAINER:

1) BACTROSTAR is filled in a 10 ml flint glass vial with grey butyl Rubber stoppers (grey bromo butyl rubber) with flip off seal. Each vial is then packed in a carton along with its pack insert.
2) A 10 ml flint glass vial with dry sterile powder is packed in a Printed Primary Carton along with the Pack Insert. One ampoule containing 10 ml Sterile Water for Injections BP is included in this pack for reconstitution.

7. MARKETING AUTHORISATION HOLDER
Sakar Healthcare Limited
Block No. 10-13, Sarkhej-Bavla Highway, Vill: Changodar,
Dist: Ahmedabad-382213, Gujarat – INDIA.

8. MARKETING AUTHORISATION NUMBER(S)
Not Applicable

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION
Not Applicable

10. DATE OF REVISION OF THE TEXT
Not Applicable