SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of The Medicinal Product:

TRAXOL-S (Ceftriaxone & Sulbactam for Injection 1500 mg)

2. Qualitative and quantitative composition:

Each vial contains:

Ceftriaxone Sodium USP (Sterile)

Equivalent to Ceftriaxone 1000 mg

Sulbactam Sodium USP (Sterile)

Equivalent to Sulbactam 500 mg

S. No.	Name of Material	Specification	Label Claim	Qty/Vial (In mg)	Function
1.	**Ceftriaxone Sodium (Sterile)**	**USP**	**1000 mg**	**1193.571***	**Active Ingredient**
2.	**Sulbactam Sodium (Sterile)**	**USP**	**500 mg**	**542.698***	**Active Ingredient**

***** Actual fill weight is based on QC results of Assay and water content of the API used.

3. Pharmaceutical Form: Dry Powder for Injection.

4. CLINICAL PARTICULARS

4.1 Indications and Usage

Traxol-S is Indicated for the treatment of following infections when caused by susceptible bacteria.

1. Meningitis
2. For treatment of Nosocomial infections surgical prophylaxis
3. Urinary tract infections (complicated by underlying urological abnormalities)
4. skin and soft tissue infections Like cellulites, erysipelas etc.
5. Cholecystitis
6. Osteomyelitis
7. Sexually transmitted diseases (Gonorrhoea, Chancroid, Syphilis)

8. Chronic suppurative bacterial otitis media
9. Infections in dialysis unit

The preoperative administration of Traxol-S may reduce the Incidence of postoperative Infections In patients undergoing surgical procedures.

4.2. Posology and method of administration

TRAXOL-S may be administered Intravenously 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 infection. The total daily dose should not exceed 4 grams.

For the treatment of uncomplicated gonococcal Infections, a single Intramuscular dose of 250 mg is recommended.

For preoperative use (surgical prophylaxis), a single dose of 1 gram administered Intravenously ½ to 2 hours before surgery is recommended.

In the treatment of meningitis, it is recommended that the initial therapeutic dose be 100 mg/Kg (not to exceed 4 grams). Thereafter a total daily dose of 100 mg/Kg/day (not to exceed 4 grams daily) is recommended. The daily dose may be administered once a day (or in equally divided doses every 12 hours). The usual duration of therapy is 7 to 14 days.

Generally, TRAXOL-S therapy should be continued for at least 2 days after the signs and symptoms of infection have disappeared.

The usual duration of therapy is 4 to 14 days in complicated infection, longer therapy may be required. When treating infections caused by Streptococcus pyogenes. therapy should be continued for at least 10 days.

No dosage adjustment is necessary for patients with impairment of renal or hepatic function; however, blood levels should be monitored in patients with severe renal impairment (e.g., dialysis patients) and in patients with both renal and hepatic dysfunctions.

Children: For the treatment of skin and skin structure infections, the recommended total daily dose is 50 to 75 mg/kg given once a day (or in equally divided doses twice a day). The total daily doses should not exceed 2 grams.

For the treatment of acute bacterial otitis media, a single intramuscular dose of 50 mg/kg (not to exceed 1 gram) is recommended.

For the treatment of serious miscellaneous infections other than meningitis, the recommended total daily dose is 50 to 75 mg/given in divided doses every 12 hours. The total daily dose should not exceed 2 grams.

4.3. Contraindications

Ceftriaxone Injection is contraindicated in patients with known hypersensitivity to cephalosporin antibiotics. In patients hypersensitive to penicillin, consider the possibility of allergic cross-reactions.

The use of sulbactam is contraindicated in individuals with a history of hypersensitivity reactions to any of the penicillins.

4.4. Special Warning and Precautions for use

Serious or occasionally fatal anaphylactic reactions have been reported in patients receiving beta-lactam antibiotics. These reactions are more likely to occur in individuals with a history of hypersensitivity reactions to multiple allergens. 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.

General

Transient elevations of BUN and serum creatinine have been observed, at recommended doses, the nephrotoxic potential of ceftriaxone is same as other cephalosporins. Since Ceftriaxone is excreted both via renal and bile patients with renal failure normally require no adjustment in dosage when usual doses of Ceftriaxone are administered. Dosage adjustments are not necessary in patients with hepatic dysfunction.

However, in patients with both renal failure and hepatic dysfunction, dosage should not exceed more than 2 g daily with close monitoring of serum concentrations.

4.5. Interaction with other medicinal products and other forms of interaction

Alcohol: A possible disulfram like reaction with alcohol, though the potential for this and hypoprothrombinaemia is low because of the N-methylthiotetrazole side chain present in cephamandole.

4.6. Pregnancy and lactation

Teratogenic effects: Pregnancy category B. As per published data, 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 teratogenicity. In primates no teratogenicity 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.

Nursing Mothers

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.

4.7. Effects on ability to drive and use machines

Ceftriaxone has been associated with dizziness, which may affect the ability to drive or operate machinery.

4.8. Undesirable Effects

Clinical studies of the combination of sulbactam plus beta-lactam antibiotics or penicillins have revealed no major hematologic, renal, hepatic, or central nervous system reactions. Diarrhea has not been a major problem after intravenous use.

Incidence of side-effects due to Ceftriaxone is as follows: G.I. effects- 2-3%,
cutaneous reactions 1-3%, hematological 1-2%, miscellaneous 1.5-3%

4.9. Overdose

In the case of overdose nausea, vomiting, diarrhoea, can occur. Ceftriaxone concentration cannot be reduced by haemodialysis or peritoneal dialysis. There is no specific antidote. Treatment is symptomatic.

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties:

ATC Classification: Ceftriaxone, combinations

ATC Code: J01DD54

Mode of action

The bactericidal activity of Traxol S 1.5 g is due to the Ceftriaxone component and the ability of Ceftriaxone to interfere with the biosynthesis of the peptidoglycan component of the bacterial cell wall by binding to and inactivating penicillin-binding proteins (PBPs). Ceftriaxone induces filamentation in Escherichia coli and Pseudomonas aeruginosa, it binds primarily to PBP 3 which is responsible for formation of cross-wall or septum of dividing bacilli. Ceftriaxone has a high degree of stability against the beta-lactamases, both penicillinases and cephalosporinases produced by both gram -ve and gram +ve bacteria but not against chromosomally and plasmid mediated ESBL's produced by some strains of Klebsiella, Escherichia coli, Enterobacter spp and Serratia spp.

Sulbactam irreversibly blocks the destruction of beta-lactam ring of Ceftriaxone by these wide variety of ESBLs and chromosomally mediated beta-lactamases by attaching to these enzymes and acting as a suicide substrate that forms a stable intermediate, rendering the enzyme inactive. Sulbactam is a broader-spectrum beta-lactamase inhibitor than clavulanic acid. Sulbactam does not induce chromosomal beta-lactamases like clavulanic acid, nor does it select for derepressed beta-lactamase-producing bacteria. Thus the full potential of Ceftriaxone against Klebsiella, pseudomonas, Escherichia coli spp is restored by addition of Sulbactam. Impaired renal function and Hepatic insufficiency: Ceftriaxone is excreted via both renal and biliary pathways therefore patients with renal failure normally require no adjustments of dose however concentration of the drug should be monitored in such patients and if there is evidence of drug accumulation then dosage adjustments should be made accordingly. Dosage adjustments are not necessary in patients with hepatic dysfunction, however in patients with both hepatic dysfunction and significant renal failure, dosage should not exceed more than 2 gm daily with close monitoring of serum concentrations

5.2 Pharmacokinetics Properties

Following intramuscular administration, peak serum concentrations of Ceftriaxone and Sulbactam are seen between 15 minutes to 2 hrs. The maximum plasma conc of Ceftriaxone after a single IM dsoe of 1.0 g is about 81mg/L and is reached 2-3 hrs after the dose while that of Sulbactam sodium is 6-24 mg/L and is reached approximately 1 hr after the dose. Hence effective amount of beta-lactamases are destroyed by the time peak concentration of Ceftriaxone is reached allowing full potential of action of Ceftriaxone against ESBL producing Klebsiella, E coli spp. Serum concentrations have been shown to be proportional to the amount of dose administered. 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. The concentrations in most extracellular foci reach or exceed several times the MIC of most pathogens for at least 24 hours after a single administration. Ceftriaxone sodium reaches therapeutically effective concentrations in patients with bacterial meningitis which are at least ten-fold the MICs of common pathogens such as, Enterobacteriaceae, H. influenzae, Meningococci, Pneumococci and Group B Streptococci.

Ceftriaxone crosses placenta and is distributed in the amniotic fluid. It is also distributed in the milk.

Metabolism and excretion

Ceftriaxone is not metabolised in the body and is eliminated unchanged via two pathways, urine and bile. 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.

Metabolism of sulbactam is less than 25%. 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. Impaired renal function and Hepatic insufficiency: Ceftriaxone is excreted via both renal and biliary pathways therefore patients with renal failure normally require no adjustments of dose however concentration of the drug should be monitored in such patients and if there is evidence of drug accumulation then dosage adjustments should be made accordingly. Dosage adjustments are not necessary in patients with hepatic dysfunction, however in patients with both hepatic dysfunction and significant renal failure, dosage should not exceed more than 2 gm daily with close monitoring of serum concentrations.

5.3 Preclinical safety Data:

There are no pre-clinical data of relevance.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients:

Not Applicable

6.2 Incompatibilities:

None

6.3 Shelf life:

24 Months.

6.4 Special precautions for storage:

Store in dry place, below 30° C. Protect from light. Keep out of reach of children.

6.5 Nature and contents of container:

1 Vial =

Primary packing: Finished product packed in a glass vial plugged with grey butyl rubber stopper & sealed with a plain flip off aluminum seal.

Secondary packing: 20 ml Glass vial along with pack insert packed in printed carton.

6.6. Special precautions for disposal:

None

7. MARKETING AUTHORIZATION HOLDERS

CACHET PHARMACEUTICALS PVT. LTD

415, Shah Nahar, Worli, Mumbai 400 018. India.

8. MARKETING AUTHORIZATION NUMBER

09083/09160/NMR/2021

9. DATE OF FIRST AUTHORIZATION/ RENEWAL OF THE AUTHORIZATION

Oct 31, 2023

10. DATE OF REVISION OF THE TEXT

Not applicable