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

# MAXIZONE SB

## 1. Generic Name

Ceftriaxone and Sulbactam for Injection I.P. 1.5 gm and Sterile Water for Injection I.P. 10 ml.

## 2. Qualitative and quantitative Composition:

**MAXIZONE SB**

Each combipack Contains:

**1**. Ceftriaxone and Sulbactam for injection 1.5 gm

Each vial contains:

Ceftriaxone Sodium I.P. (Sterile)

equivalent to Ceftriaxone……..1000 mg

Sulbactam Sodium I.P. ( sterile)

equivalent to Sulbactam……500 mg

**2**. Sterile Water for injections I.P. 10 ml

Each ampoule Contains:

Sterile Water for Injections I.P….10 ml

## 3. Dosage form and strength

**Dosage form**: Injection

**Strength**: Ceftriaxone and Sulbactam for Injection I.P. 1.5 gm and Sterile Water for Injection I.P. 10 ml.

## 4. Clinical particulars

### 4.1. Therapeutic indication

It is indicated for treatment of LRTI.

### 4.2. Posology and method of administration

***Posology***

**Dosage:**

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).

Pediatric patients

For treatment of serious infections: Recommended total daily dose in terms of Ceftriaxone is 50-75 mg/kg given in divided doses every 12 hours. The total daily dose (in terms of Ceftriaxone) should not exceed more than 2 grams.

When treating infection caused by Streptococcus pyrogens, therapy should be continue for at least 10 days.

***Method of administration***

Dissolve the contents of the vial in 4 ml of Sterile water for Injection I.P. for IM use or 8.5 ml for IV use. Prick the ampoule of Sterile.

Water for Injection only once & discard the ampoule.

The reconstituted solution should be used immediately and not to be frozen.

There is no relevant use of abiraterone in the paediatric population.

## 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 warnings and precautions for use

**Caution:** If any foreign particle is visible in the vial after dissolving the contents, please do not use the solution and return the vial for free replacement.

**Warnings:**

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.

Pseudo membranous 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.

**Precautions:**

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 2g daily with close monitoring of serum concentrations.

## 4.5. Drugs interactions

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.

Unlike many cephalosporins, probenecid does not affect the renal excretion of Ceftriaxone.

**4.6. Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)**

**Pregnancy and Lactation:**

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 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 is 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**

During treatment with ceftriaxone, undesirable effects may occur (e.g. dizziness), which may influence the ability to drive and use machines. Patients should be cautious when driving or operating machinery.

**4.8. Undesirable effects**

- The most frequent adverse drug reactions are inflammation at injection site with pain and tenderness.
- Other common adverse drug reactions that can occur with the combination are hypersensitivity including pruritus, fever or chills.
- Common gastrointestinal side effects include, diarrhea, nausea and vomiting.
- Other side effects: Hematological complications, Elevation of hepatic enzymes, elevation of BUN, headache, dizziness, vaginitis, flatulence, dyspepsia, palpitations and epistaxis.

**Reporting of adverse reactions**

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: https://www.torrentpharma.com/index.php/site/info/adverse_event_reporting by reporting side effects, you can help provide more information on the safety of this medicine.

**4.9. Overdose**

In case of overdose, drug concentration would not be reduced by hemodialysis or peritoneal dialysis. There is no specific antidote. Treatment of overdosage should be symptomatic.

**5. Pharmacological properties**

**5.1. Mechanism of action:**

The combination of Ceftriaxone (3rd generation cephalosporin) and Sulbactam (beta-lactamase inhibitor) provides a solution for treatment of such bacterial infections caused betalactam resistant pathogens. Ceftriaxone and Sulbactam is indicated for the treatment of

following infection when caused by susceptible bacteria: Cholecystitis, Sexually transmitted diseases (Chancroid, Syphilis), Infections in dialysis unit, Lower respiratory tract infection.

**5.2. Pharmacodynamic properties:**

The bactericidal activity of Ceftriaxone & Sulbactam 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, Eschericia coli spp is restored by addition of Sulbatam.

**5.3. Pharmacokinetic properties**

Ceftriaxone and Sulbactam can be administered IM or IV.

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 dose 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 up to 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 haemodialysis. 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.

## 6. Nonclinical properties

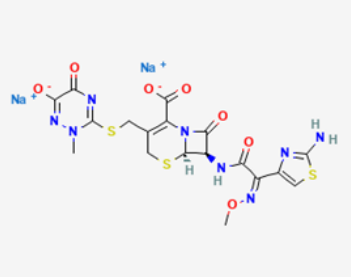
### 6.1. Animal Toxicology or Pharmacology

There are no information on Nonclinical properties.

## 7. Description

**Ceftriaxone Sodium**

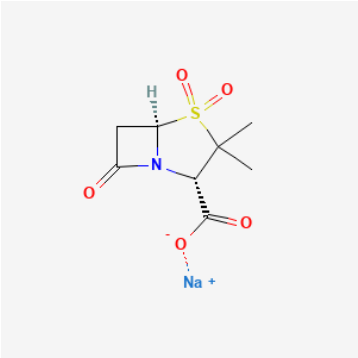
Ceftriaxone sodium is disodium (6R,7R)-7-[[(Z)-(2-aminothiazol-4-yl) (methoxyimino) acetyl]amino]-3-[[(2-methyl-6-oxido-5-oxo-2,5-dihydro-1,2,4-triazin-3-l)sulphanyl]methyl]-8-oxo-5-thi-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate hemiheptahydrate. It has empirical formula of $C_{18}H_{16}N_8Na_2O_7S_3$. 3 1/2 $H_2O$ and molecular weight of 662.0. The chemical structure is as below:



Ceftriaxone sodium is a white or yellowish, crystalline powder, slightly hygroscopic.

**Sulbactam Sodium**

Sulbactum sodium is sodium; (2S,5R)-3,3-dimethyl-4,4,7-trioxo-4λ6-thia-1-azabicyclo [3.2.0] heptane-2-carboxylate. It has empirical formula of $C_8H_{10}NNaO_5S$ and molecular weight of 255.23. The chemical structure is as below:




It is a white or almost white, hygroscopic, crystalline powder.

**MAXIZONE SB** is an off white to pale yellow crystalline powder.

## 8. Pharmaceutical particulars

### 8.1. Incompatibilities

Not applicable

### 8.2. Shelf-life

Do not use later than the date of expiry.

### 8.3. Packaging information

MAXIZONE SB is available in vial

### 8.4. Storage and handing instructions

Store protected from light, at temperature not exceeding 30°C.

Keep all medicines out of reach of children.

## 9. Patient Counselling Information

Ask the patients to inform the treating physicians in case of any of the below:

- Have any allergies
- Have kidney or liver problems
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have any serious illness
- Are taking any medicines (prescription, over-the-counter, vitamins, or herbal products)

## 10. Details of manufacturer

**Manufactured by:**

Prosperity 6 Pharmaceutics

Plot No. 23, E.P.I.P., Phase-II, Thana, Baddi-173205, Distt. Solan, (H.P)

## 11. Details of permission or licence number with date

MB/09/756 issued on 29.01.2021

## 12. Date of revision

JUL 2024

**MARKETED BY**


TORRENT PHARMACEUTICALS LTD.

**IN/MAXIZONE SB /JUL-2024/02/PI**