Summary of Product Characteristics

1. Name of the Finished Pharmaceutical Product

ALCEF-SB (Ceftriaxone Sodium & Sulbactam for Injection 1.5g)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pack contains:

Part-I

Each vial contains:

Sterile Ceftriaxone Sodium USP

Eq. to Ceftriaxone 1g

SulbactamSodium USP

Eq. toSulbactam500mg

Part-II

Sterile Water for Injection USP 10ml

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Dry powder for Injection.

Visual/ Physical description of FPP: A white to off white, crystalline powder filled in transparent glass vial.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Infections caused by pathogens sensitive to Ceftriaxone & Sulbactam for Injection, e.g.:

- Sepsis;
- Meningitis;
- Abdominal infections (peritonitis, infections of the biliary and gastrointestinal tracts);
- Infections of the bones, joints, soft tissue, skin and of wounds;
- Infections in patients with impaired defense mechanisms;
- Renal and urinary tract infections;

- Respiratory tract infections, particularly pneumonia, and ear, nose and throat infections;
- Genital infections, including gonorrhea.
- Perioperative prophylaxis of infections.
-Considerations should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and Method of Administration

The recommended *adult dosage* is 1.5 g (1 g Ceftriaxone as the sodium salt plus 0.5 g Sulbactam as the sodium salt) to 3 g (2 g Ceftriaxone as the sodium salt plus 1 g Sulbactam as the sodium salt) every six hours. This 1.5 to 3 g range represents the total of Ceftriaxone content plus the Sulbactam content and corresponds to a range of 1 g Ceftriaxone /0.5 g Sulbactam to 2 g Ceftriaxone /1 g sulbactam. The total dose of Sulbactam should not exceed 4 grams per day.

Neonates, infants and children up to 12 years:

The following dosage schedules are recommended for once daily administration. Neonates (up to 14 days): 20 to 50 mg/kg bodyweight once daily. The daily dose should not exceed 50 mg/kg. It is not necessary to differentiate between premature and term infants. Infants and children (15 days to 12 years): 20 to 80 mg/kg once daily. For children with bodyweights of 50 kg or more, the usual adult dosage should be used. Intravenous doses of NLT 50 mg/kg bodyweight should be given by infusion over at least 30 minutes.

Reconstitution or the preparation for use:

Dissolve the contents in 10 ml of sterile water for injection USP provided with this vial & Inject slowly within 3 to 5 minutes. The reconstituted solution should be used immediately after preparation.

Method of administration

Route of Administration: Intramuscular Injection/ slow Intravenous Injection.

4.3 Contra-indications

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 Sulbactamis contraindicated in individuals with a history of hypersensitivity reactions to any of the penicillins.

4.4 Special Warnings and Special Precautions for Use

This product should be given cautiously to penicillin-sensitive patients. Serious acute hypersensitivity reactions may require the use of subcutaneous epinephrine and other emergency measures.

Clostridium difficile associated diarrhea has been reported with nearly all antibacterial agents, including ceftriaxone/Sulbactam, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

An immune mediated hemolytic anemia has been observed in patients receiving cephalosporin class anti-bacterial including Ceftriaxone. If a patient develops anemia while on ceftriaxone, the diagnosis of a cephalosporin associated anemia should be considered and ceftriaxone stopped until the etiology is determined.

Although transient elevations of BUN and serum creatinine have been observed, at the recommended dosages, the nephrotoxic potential of ceftriaxone/ Sulbactamis similar to that of other cephalosporins.

Alterations in prothrombin times have occurred infrequently in patients treated with ceftriaxone/Sulbactam. Patients with impaired vitamin K synthesis or low vitamin K stores (eg, chronic hepatic disease and malnutrition) may require monitoring of prothrombin time during Ceftriaxone and Sulbactamtreatment. It should also be prescribed with caution in individuals with a history of gastrointestinal disease, especially colitis. There have been reports of sonographic abnormalities in the gall bladder of patients treated with ceftriaxone/Sulbactam; some of these patients also had symptoms of gall bladder disease.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

Calcium-containing diluents, such as Ringer's solution or Hartmann's solution, should not be used to reconstitute Rocephin vials or to further dilute a reconstituted vial for intravenous administration because a precipitate can form. Precipitation of ceftriaxone-calcium can also occur when ceftriaxone is mixed with calcium-containing solutions in the same intravenous administration line. Ceftriaxone must not be administered simultaneously with calcium-containing intravenous solutions, including continuous calcium-containing infusions such as parenteral nutrition via a Y-site. However, in patients other than neonates, ceftriaxone and calcium-containing solutions may be administered sequentially of one another if the infusion lines are thoroughly flushed between infusions with a compatible fluid. *In vitro* studies using adult and neonatal plasma from umbilical cord blood demonstrated that neonates have an increased risk of precipitation of ceftriaxone-calcium.

Concomitant use with oral anticoagulants may increase the anti-vitamin K effect and the risk of bleeding. It is recommended that the International Normalised Ratio (INR) is monitored frequently and the posology of the anti-vitamin K drug adjusted accordingly, both during and after treatment with ceftriaxone.

There is conflicting evidence regarding a potential increase in renal toxicity of aminoglycosides when used with cephalosporins. The recommended monitoring of aminoglycoside levels (and renal function) in clinical practice should be closely adhered to in such cases.

In an *in-vitro* study antagonistic effects have been observed with the combination of chloramphenicol and ceftriaxone. The clinical relevance of this finding is unknown.
There have been no reports of an interaction between ceftriaxone and oral calcium-containing products or interaction between intramuscular ceftriaxone and calcium-containing products (intravenous or oral).

In patients treated with ceftriaxone, the Coombs' test may lead to false-positive test results.
Ceftriaxone, like other antibiotics, may result in false-positive tests for galactosaemia.

Likewise, non-enzymatic methods for glucose determination in urine may yield false-positive results. For this reason, glucose level determination in urine during therapy with ceftriaxone should be carried out enzymatically.

No impairment of renal function has been observed after concurrent administration of large doses of ceftriaxone and potent diuretics (e.g. furosemide).
Simultaneous administration of probenecid does not reduce the elimination of ceftriaxone.

4.6 Fertility, pregnancy and lactation

Pregnancy

Category B: Either animal-reproduction studies have not demonstrated a foetal risk but there are no controlled studies in pregnant women or animal-reproduction studies have shown an adverse effect (other than a decrease in fertility) that was not confirmed in controlled studies in women in the 1st trimester (and there is no evidence of a risk in later trimesters).

Lactation

Caution when used during lactation.

Fertility

Reproductive studies have shown no evidence of adverse effects on male or female fertility.

4.7 Effects on Ability to Drive and Use Machines

If you experience drowsiness, dizziness, hypotension or a headache as side-effects when using Ceftriaxone SulbactamInjection medicine then it may not be safe to drive a vehicle or operate heavy machinery. One should not drive a vehicle if using the medicine makes you drowsy, dizzy or lowers your blood-pressure extensively. Pharmacists also advise patients not to drink alcohol with medicines as alcohol intensifies drowsiness side-effects. Please check for these effects on your body when using Ceftriaxone SulbactamInjection. Always consult with your doctor for recommendations specific to your body and health conditions.

Undesirable Effects

The most frequently reported adverse reactions for ceftriaxone are eosinophilia, leucopenia, thrombocytopenia, diarrhoea, rash, and hepatic enzymes increased.

Data to determine the frequency of ceftriaxone ADRs was derived from clinical trials.

The following convention has been used for the classification of frequency:

Very common (≥ 1/10)

Common (≥ 1/100 - < 1/10)

Uncommon (≥ 1/1000 - < 1/100)

Rare (≥ 1/10000 - < 1/1000)

Not known (cannot be estimated from the available data)

System Organ Class	Common	Uncommon	Rare	Not Known [a]
Infections and infestations		Genital fungal infection	Pseudo-membranous colitis[b]	Superinfection[b]
Blood and lymphatic system disorders	Eosinophilia Leucopenia Thrombocytopenia	Granulocytopenia Anaemia Coagulopathy		Haemolyticanaemia[b] Agranulocytosis
Immune system disorders				Anaphylactic shock Anaphylactic reaction Anaphylactoid reaction Hypersensitivity[b] Jarisch-Herxheimerreaction[b]
Nervous system disorders		Headache Dizziness	Encephalopathy	Convulsion
Ear and				Vertigo

labyrinth disorders				
Respiratory, thoracic and mediastinal disorders			Bronchospasm	
Gastrointestinal disorders	Diarrhoea[b] Loose stools	Nausea Vomiting		Pancreatitis[b] Stomatitis Glossitis
Hepatobiliary disorders	Hepatic enzyme increased			Gall bladder precipitation[b] Kernicterus
Skin and subcutaneous tissue disorders	Rash	Pruritus	Urticaria	Stevens Johnson Syndrome[b] Toxic epidermal necrolysis[b] Erythema multiforme Acute generalisedexanthematous pustulosis Drug reaction with eosinophilia and systemic symptoms (DRESS)[b]
Renal and urinary disorders			Haematuria Glycosuria	Oliguria Renal precipitation (reversible)
General disorders and administration site conditions		Phlebitis Injection site pain Pyrexia	Oedema Chills	
Investigations		Blood creatinine increased		Coombs test false positive[b]

				Galactosaemia test false positive[b] Non enzymatic methods for glucose determination false positive[b]

[a] Based on post-marketing reports. Since these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency which is therefore categorised as not known.

Description of selected adverse reactions

Infections and infestations

Reports of diarrhoea following the use of ceftriaxone may be associated with *Clostridium difficile*. Appropriate fluid and electrolyte management should be instituted.

Ceftriaxone-calcium salt precipitation

Rarely, severe, and in some cases, fatal, adverse reactions have been reported in pre-term and full-term neonates (aged < 28 days) who had been treated with intravenous ceftriaxone and calcium. Precipitations of ceftriaxone-calcium salt have been observed in lung and kidneys post-mortem. The high risk of precipitation in neonates is a result of their low blood volume and the longer half-life of ceftriaxone compared with adults.

Cases of ceftriaxone precipitation in the urinary tract have been reported, mostly in children treated with high doses (e.g. ≥ 80 mg/kg/day or total doses exceeding 10 grams) and who have other risk factors (e.g. dehydration, confinement to bed). This event may be asymptomatic or symptomatic, and may lead to ureteric obstruction and postrenal acute renal failure, but is usually reversible upon discontinuation of ceftriaxone.

Precipitation of ceftriaxone calcium salt in the gallbladder has been observed, primarily in patients treated with doses higher than the recommended standard dose. In children, prospective studies have shown a variable incidence of precipitation with intravenous application - above 30 % in some studies. The incidence appears to be lower with slow infusion (20 - 30 minutes). This effect is usually asymptomatic, but the precipitations have been accompanied by clinical symptoms such as pain, nausea and vomiting in rare cases. Symptomatic treatment is recommended in these cases. Precipitation is usually reversible upon discontinuation of ceftriaxone.

Overdose

Symptoms: In the case of Ceftriaxone overdose nausea, vomiting, diarrhoea, can occur. Ceftriaxone concentration cannot be reduced by haemodialysis or peritoneal dialysis.

Treatment: There is no specific antidote. Treatment is symptomatic.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic Properties

Pharmacotherapeutic group: Third generation cephalosporins;

ATC code: J01DD54.

Ceftriaxone Sulbactam Injection improves the patient's condition by performing the following functions:

Preventing destruction antibiotics, from chemicals released from bacteria.

Inhibiting the bacterial cell wall synthesis.

Ceftriaxone is a 2-aminothiazolyl methoxylmino third-generation cephalosporin derivative. Ceftriaxone, a bactericidal antimicrobial, inhibits bacterial cell wall synthesis of actively dividing cells by binding to one or more penicillin-binding proteins (PBPs). These proteins are associated with the bacterial cell membrane and probably serve in synthesis. The result is the formation of a defective cell wall that is osmotically unstable. Bacterial species have a unique set of PBPs. The affinity pattern of ceftriaxone for the PBPs for different bacterial species affects the drug's antimicrobial spectrum of activity. It is also felt that cephalosporins, as well as penicillins, may increase the breakdown of the cell wall of the bacteria by decreasing the availability of an inhibitor of murein hydrolase, an enzyme involved in cell division. If unimposed, this enzyme can destroy the integrity of the cell wall.

Sulbactam does not possess any useful antibacterial activity, except against Neisseriaceae and Acinetobacter. AsSulbactam also binds with some penicillin-binding proteins, sensitive strains are also often rendered more susceptible to Sulbactam/Ceftriaxone than to Ceftriaxone alone. The combination of Sulbactamand Ceftriaxone is active against all organisms sensitive to ceftriaxone.

5.2 Pharmacokinetic Properties

Absorption:

Ceftriaxone: 98% bound to plasma proteins; crosses the blood brain barrier. After 500 mg IVSulbactam are 21-40 mcg/ml and 48-88 mcg/ml respectively.

Metabolism and Excretion:

Ceftriaxone: Elimination half-life is about 8.7 hours; 33-67% removed as unchanged drug. About 75-85% of Sulbactam is excreted in the urine during the first eight hours of administration.

5.3 Preclinical Safety Data

Clinical studies revealed that the combination of Ceftriaxone and Sulbactam had no major problem after intravenous use. Incidence of side-effects due to Ceftriaxone is very negligible.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

None

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 4.2

6.3 Shelf Life

Product as packaged for sale: 36 Months

Following reconstitution: 24 hours

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would not be longer than the times stated above for the chemical and physical in-use stability.

6.4 Special Precautions for Storage

Do not store above 30°C. Keep the vial in the outer carton in order to protect from light.

Following reconstitution: 2°C-8°C.

6.5 Nature and Contents of Container

20 ml clear, transparent vial of Ceftriaxone Sodium & Sulbactamfor injection & 10 ml sterile water for injection USP is packed in a unit carton along with Leaflet.

6.6 Special precautions for disposal and other handling

This product is for single use only.

After 24 hours any unused solution should be discarded.

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

Physical description of the product after reconstitution: A clear colorless solution appears after reconstitution.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER

TAN 22 HM 0004

9. DATE OF FIRST AUTHORISATION

10/01/2022

10. DATE OF REVISION OF THE TEXT

April, 2022.