Summary of Product Characteristics (SmPC)

1. Name of the product： Ceftriaxone Sodium for Injection 1g

Camtaxone Injection 1g

2. Qualitative and quantitative composition

Each vial contains: Ceftriaxone Sodium eq. to Ceftriaxone 1g

Inactive ingredients: None

3. Pharmaceutical form

Powder for Injection. Almost white or yellowish, crystalline powder.

4. Clinical particulars

PHARMACOLOGICAL ACTION:

Ceftriaxone is a broad-spectrum cephalosporin with a long plasma elimination half-life of approximately 8 hours in normal adults.

Antimicrobial Profile

(In vitro sensitivity does not necessarily imply in vivo efficacy).

The in vitro spectrum of activity of ceftriaxone encompasses:

(a) Gram-positive organisms:

Streptococcus pneumoniae, Streptococcus Group A (including Streptococcus pyogenes), Streptococcus Group B (including Streptococcus agalactiae), Streptococcus viridans, Streptococcus bovis (Group D), Staphylococcus aureus (methicillin sensitive). Peptostreptococcus sp., and Clostridium sp.

Note: Methicillin-resistant Staphylococcus spp. are resistant to ceftriaxone. Enterococcus faecalis, Enterococcus faecium and Listeria monocytogenes are resistant.

(b) Gram-negative organisms:

Haemophilus influenzae (including ampicillin-resistant strains), Haemophilus parainfluenzae, Neisseria meningitidis, Neisseria gonorrhoeae (including penicillin-resistant strains),Escherichia coli, Klebsiella sp**, Enterobacter sp*, Serratia marcescens, Citrobacter sp., Proteus mirabilis, Indole-positive Proteus (including Morganella morganii), Salmonella sp., Shigella sp., Yersinia pestis and Treponema pallidum (in animal experiments).

*Some isolates of these species are resistant to ceftriaxone, due to the production of the chromosomally encoded beta-lactamases.

**Some isolates of these species are resistant due to production of extended spectrum plasmid mediated beta-lactamase.

(c) Organisms which are only partially sensitive to ceftriaxone in vitro. Staphylococcus epidermidis, Pseudomonas aeruginosa, Acinetobacter sp. and Bacteroides sp. Ceftriaxone is stable in relation to the majority of beta-lactamases.

The following organisms are resistant:

Ureaplasma urealyticum, Mycoplasma sp., Mycobacterium sp., Fungi.

It is essential to note that recommended media (free from inhibitory substances especially thymidine and thymine) and methods must be used for satisfactory sensitivity testing.

【Indications】

Infections caused by pathogens sensitive to ceftriaxone such as

- Sepsis
- Meningitis in neonates and infants
- perioperative prophylaxis of infections

- Renal and urinary tract infections

- Respiratory tract infections, particularly pneumonia, and ear, nose and throat infections.

- Infections of the bones, joints, soft tissue, skin and of wounds.

- Abdominal infections (peritonitis, infections of the biliary tract).

- Uncomplicated gonorrhoea

5. Pharmacological properties

【Usage and dosage】

Standard dosage

Adults and children over twelve: 1-2g ceftriaxone once daily (every 24 hours).

In severe infections and in cases in which the pathogens are only moderately sensitive to ceftriaxone, the daily dosage may be increased to 4 g administered daily.

Infants and young children may receive from 20-80 mg per kg body-mass daily; depending on the severity of the infection, usually 12-24 hourly.

In cases of premature babies, the daily dosage should not exceed 50 mg per kg body mass on account of the immaturity of the infant's enzyme systems.

Elderly patients: The dosages recommended for adults require no modification in the case of geriatric patients.

Duration of therapy: The duration of therapy varies according to the course of the disease. Administration of ceftriaxone should be continued for a minimum of 48 to 72 hours after the patient has become afebrile or evidence of bacterial eradication has been obtained.

Special dosage instructions: Meningitis: In bacterial meningitis in neonates and children, treatment begins with doses of 100 mg per kg (not to exceed 4 g) once daily. As soon as the causative organism has been identified and its sensitivity determined, the dosage can be reduced accordingly.

Gonorrhoea: For the treatment of gonorrhoea (penicillinase-producing and non-penicillinase- producing strains), a single IM dose of 250 mg ceftriaxone is recommended.

Perioperative prophylaxis: A single dose of 1-2 g ceftriaxonea dministered 30-90 minutes prior to surgery. In colorectal surgery, concurrent (but separate) administration of ceftriaxone with a 5-nitroimidazole, eg. ornidazole, has proven effective.

Impaired renal and hepatic function: In patients with impaired renal function, there is no need to reduce the dosage ofceftriaxoneprovided that the hepatic function is intact.

In case of severe renal failure (creatinine clearance <10 mL/min) the ceftriaxone dosage should not exceed 2 g daily. In patients with liver damage, there is no need for the dosage to be reduced provided renal function is intact.

In cases of concomitant severe renal and hepatic dysfunction, the plasma concentrations of ceftriaxone should be determined at regular intervals. In patients undergoing dialysis no additional supplementary dosing is required following the dialysis. Serum concentrations should be monitored, however, to determine whether dosage adjustments are necessary, since the elimination rate in these patients may be reduced.

Intramuscular Injection

For IM injection, Ceftriaxone 250 should be dissolved in 2 mL and Ceftriaxone1 g in 3.5 mL of water for injection. Ceftriaxone dissolved in a 1% lidocaine solution can reduce pain at the site of injection. Ceftriaxone must be injected well within the body of a relatively large muscle. It is recommended that not more than 1 g be injected on

either side. Reconstitution with 1% lidocaine (without adrenaline) has no effect on the absorption or the elimination of Ceftriaxone. The lidocaine solution must never be administered intravenously.

Intravenous Injection

For IV injection, Ceftriaxone 250 is dissolved in 5 mL water for injection and Ceftriaxone 1 g dissolved in 10 mL water for injection. The intravenous administration should be given over two to four minutes.

Intravenous infusion

The infusion should be given over a period of at least 30 minutes. For IV infusion, 2 g of Ceftriaxone is dissolved in approximately 40 mL of sterile water for injection.

Ceftriaxone solutions should not be mixed with or piggybacked into solutions containing other antimicrobial drugs or into diluent solutions other than those listed above, owing to possible incompatibility.

Incompatibilities: Ceftriaxone should not be added to solutions containing calcium such as Hartmann's solution and Ringers solution. Ceftriaxone is incompatible with amsacrine, vancomycin and fluconazole and aminoglycosides.

Side effects

Systemic:

Gastro-intestinal complaints: Loose stools/diarrhoea, nausea, vomiting, stomatitis, glossitis.

Haematological changes: Eosinophilia, haematoma or bleeding, thrombocytopenia, neutropenia, leukopenia, granulocytopenia and haemolytic anaemia.

Isolated cases of agranulocytosis ($<500/mm^3$) have been reported, most of them following total doses of 20 g or more.

Exanthema, allergic dermatitis, pruritus, urticaria, oedema, erythema multiforme may occur.

Other side effects include headaches and dizziness, increase in liver enzymes, oliguria, increase in serum creatinine, mycosis of the genital tract, fever, shivering and anaphylactic or anaphylactoid reactions.

Nephrotoxicity has been reported. Acute interstitial nephritis is also a possibility as a manifestation of hypersensitivity.

Anaphylactic shock may occur: Anaphylactic shock requires immediate counter measures.

Acute renal tubular necrosis has followed excessive dosage and has also been associated with the use of Ceftriaxone in older patients or those with pre-existing renal impairment, or with the concomitant administration of nephrotoxic agents such as aminoglycosides.

Hepatitis and cholestatic jaundice have occurred less frequently.

Prolonged use may result in overgrowth of non-susceptible organisms.

Pseudomembranous colitis has been reported with Ceftriaxone. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of Ceftriaxone. Superinfections with non-susceptible micro-organisms may occur.

Local

Inflammatory reactions in the vein wall may occur after IV administration. These may be minimised by slow (2-4 minutes) injection of Ceftriaxone.

Intramuscular injection without lidocaine solution is painful.

Shadows which have been mistaken for gall stones have been detected by sonograms of the gallbladder, usually following higher than the standard recommended dose.

These shadows are, however, precipitates of calcium ceftriaxone which disappear on completion or discontinuation of ceftriaxone therapy.

In less frequent cases, these findings have been associated with symptoms. In symptomatic cases, conservative non-surgical management is recommended. Discontinuation of Ceftriaxone treatment in symptomatic cases should be at the discretion of the clinician.

Studies have shown that Ceftriaxone, can displace bilirubin from serum albumin. Caution should be exercised when considering Ceftriaxone treatment in hyperbilirubinemic neonates. Ceftriaxone should not be used in neonates (especially prematures) at risk of developing bilirubin encephalopathy.

During prolonged treatment the blood profile should be checked at regular intervals

Renal and haemotological status should be monitored especially during prolonged and high dose therapy.

Interactions:

No impairment of renal function has been observed after concurrent administration of large doses of Ceftriaxone and potent diuretics (eg. furosemide). There is no evidence that Ceftriaxone increases renal toxicity of aminoglycosides. No effects similar to that of disulfiram has been demonstrated after administration of alcohol with Ceftriaxone.

Ceftriaxone does not contain an N-methyl-thiotetrazole moiety 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 and Ceftriaxone.

There may be antagonism between Ceftriaxone and bacteriostatic antibacterial agents. Ceftriaxone may interfere with the Jaffe method of measuring creatinine

concentrations and may produce falsely high values; this should be borne in mind when measuring renal function.

In patients treated with ceftriaxone the Coombs'test may become false positive. Ceftriaxone may result in false positive tests for galactosemia.

Likewise, nonenzymatic 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.

6. Pharmaceutical particulars

6.1 List of excipients

None.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in a cool and dry place below 30°C. Protect from light and moisture.

Keep all medicines out of reach of children.

6.5 Nature and contents of container

Vials.

6.6 Special precautions for disposal and other handling

The reconstituted solution should be used immediately after preparation. Any remaining part should be discarded after reconstituted.

7. Manufacturer name

Shandong Xier Kangtai Pharmaceutical Co., Ltd.

Private Economy Garden, Xinyan Town, Yanzhou, Jining City, Shandong China

8. Marketing Authority

MARK PHARMACEUTICALS LIMITED

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