Summary of Product Characteristics

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

Ceftazidime for Injection 1 g

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 1 g ceftazidime (as pentahydrate) with sodium carbonate (118 mg per gram of ceftazidime).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for solution for injection or infusion

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Ceftazidime for Injection 1.0g is indicated for the treatment of the Bacteraemia, lower respiratory infections, intra-abdominal and biliary tract infection, complicated urinary tract infections, complicated skin and soft tissue infections by Gram negative bacteria.

Ceftazidime for Injection is particularly applicable to immunodeficiency infection and nosocomial infection caused by Gram negative bacteria and the central nervous system infection caused by Gram negative bacterial or Pseudomonas aeruginosa.

4.2 Posology and method of administration

[Posology and method of administration]

Adults:

(1) For the treatment of bacteraemia, lower respiratory infections, intra-abdominal and biliary tract infection, administer 4-6 g every day in two or three divided doses of intravenous infusion or intravenous injection. The course of treatment is 10-14 hours.

(2) For the treatment of urinary tract infections, complicated skin and soft tissue infections, administer 2-4 g every day in two divided doses of intravenous infusion or intravenous injection. The course of treatment is 7-14 hours. For mild grade urinary tract infections, administer 0.5-1g every 12 hours.

(3) For the treatment of life-threatening infections, serious Pseudomonas aeruginosa infections and central nervous system infection, administer to 0.15-0.2g/kg/day in three doses of intravenous infusion or intravenous injection.

Children:

Toddlers > 2 months: 30~100 mg/kg/day, in two or three divided doses of intravenous infusions/day;

Neonates and infants ≤ 2 months: with limited clinical experience.

Patients with renal impairment: Ceftazidime is excreted unchanged by the kidneys. Therefore, in patients with impaired renal function, the dosage should be reduced. The dosage can be used based on the endogenous creatinine clearance rate. The patient should remain the dosage after dialysis.

4.3 Contraindications

Ceftazidime for injection is contraindicated in patients who have shown hypersensitivity to ceftazidime or the cephalosporin group of antibacterial drugs.

4.4 Special warnings and special precautions for use

4.4.1. Cross-allergic reaction: The patients have a history of hypersensitivity reaction to any cephalosporin or to any cephamycin are possible to have hypersensitivity reactions to other cephalosporins or to other cephamycins. The patients have a history of hypersensitivity reaction to penicillin, penicillin derivatives and penicillamine may experience cross-allergic reaction to any cephalosporin or to any cephamycin. If this product is to be given to penicillin-sensitive patients, may occur in 5-10% of patients with hypersensitivity to cephalosporin and up to 20% of patients sensitive to cephalosporin once hypersensitivity test is performed.

4.4.2. Careful inquiry should be made to determine whether the patient has hypersensitivity to penicillin. Ceftazime for injection should not be used for any patient with allergic shock or intermediate response to penicillin.

4.4.3. Pseudomembranous colitis has been reported with nearly all antibacterial agents, including ceftazidime. It is important to be used with caution in patients who present with gastrointestinal disease including ulcerative colitis, regional enteritis or colonitis related antibacterial agents.

4.4.4. There is no proof of renal toxicity for ceftazidime. The total daily dosage should be reduced when ceftazidime is administered to patients with renal insufficiency.

4.4.5. As with other antibiotics, prolonged use of Ceftazidime for Injection may result in overgrowth of nonsusceptible organisms. If super infection occurs during therapy, appropriate measures should be taken.

4.4.6. This product is not the first choice for Gram positive bacterial

4.4.7. Test changes during Ceftazidime clinical trials were transient and included: positive Coomb’s test, slight elevations in one or more of the hepatic enzymes, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, blood urea nitrogen and serum creatinine.

4.4.8. The reconstituted solution with normal saline solution, 5% glucose solution or sodium lactate for intravenous injection (20 mg/mL) should not be longer than 24 hours at room temperature.

4.4.9. The color of this product will become dark in different storage conditions and it will not affect the quality.

4.4.10. Carbon dioxide will be generated if this product is resolved by the reagent with sodium carbonate. Carbon dioxide should be released before use.

4.5. Interaction with other FPPs and other forms of interaction

1. Ceftazidime has shown to be antagonistic to amikacin sulfate, gentamicin, kanamycin, tobramycin, neomycin, chlortetracycline hydrochloride, tetracycline hydrochloride, oxybiotic, Colistimethate Sodium, polymyxin B sulfate, Erythromycin gluconate, erythromycin lactobionate, lincomycin, Sulfisoxazole, aminophylline, soluble barbiturates, calcium chloride, calcium gluconate, diphenhydramine hydrochloride and other antihistamine drugs, lidocaine,

noradrenaline, aramine, ritalin and succinylcholine. Ceftazidime has occasionally shown to be antagonistic to penicillin, methicillin, succinate hydrocortisone, dilantin, prochlorperazine, vitamin B and vitamin C, protein hydrolysate.

2. This product is less stable in sodium dicarbonate solution than in others.

3. Nephrotoxicity has been reported following concomitant administration of cephalosporins with aminoglycoside antibacterial drugs or potent diuretics such as furosemide. Renal function should be carefully monitored to avoid the potential renal impairment.

4.6. Pregnancy and lactation

Pregnancy

Reproduction studies have been performed in mice and rats at doses up to 40 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to Ceftazidime for Injection. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed

Breast-feeding

Ceftazidime is excreted in human milk. Caution should be exercised when Ceftazidime for Injection is administered to a nursing woman.

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. However, undesirable effects may occur (e.g. dizziness), which may influence the ability to drive and use machines.

4.8. Undesirable effects

Ceftazidime is generally well tolerated. The incidence of adverse reactions associated with the administration of ceftazidime was low in clinical trials. The most common adverse reactions are (1) local reactions following intravenous administration such as phlebophlogosis and thrombophlebitis; (2) allergic reactions: maculopapular or uticarcial rash, Pruritus and rare angioneurotic edema, bronchospasm and hypotension. Toxic epidermal necrolysis is rarely reported as other cephalosporins; (3) gastrointestinal reactions: nausea, vomiting, diarrhoea, abdominal pain and rare thrush and colitis. Colitis is maybe related with Clostridium difficile and will be shown as seudomembranous colitis; (4) central nervous system: headache, dizziness, paraesthesia, also epileptic seizure is rarely reported; (5) Clinical trial results: transient elevation of aspartate aminotransferase, alanine aminotransferase alkaline phosphatase. blood urea nitrogen, and/or serum creatinine were observed occasionally. Transient leukopenia, neutropenia, agranulocytosis, thrombocytopenia, and lymphocytosis were seen very rarely.

4.9. Overdose

Ceftazidime overdosage has occurred in patients with renal failure. Reactions have included seizure activity, encephalopathy, asterixis, neuromuscular excitability, and coma. Patients who receive an acute overdosage should be carefully observed and given supportive treatment. In the presence of renal insufficiency, hemodialysis or peritoneal dialysis may aid in the removal of ceftazidime from the body.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Anti-bacterials for systemic use. Third-generation cephalosporins.

Ceftazidime acts by inhibition of bacterial cell wall synthesis. Ceftazidime has activity of most Gram negative and Gram positive bacteria. Ceftazidime has high activity to Escherichia coli, Penumobacillus and other Pseudomonas spp, Haemophilus influenza and Pseudomonas aeruginosa. Ceftazidime also has good antimicrobial activity to nitrate negative bacilli and alcaligenes. Ceftazidime still has activity in the presence of some beta-lactamases of above Gram negative bacteria. Gram positive bacteria such as Pneumococcus, hemolytic streptococcus are highly sensitive to Ceftazidime and ceftazidime only has medium activity to streptococcus. Pneumococcus and methicillin-resistant staphylococci show drug resistance to Ceftazidime. Ceftazidime has some activity to the anaerobion such as peptococcus and peptostreptococcus and low activity to bacteroides fragilis.

Ceftazidime is a bactericidal agent. Ceftazidime inhibits bacterial cell wall synthesis following attachment to penicillin binding proteins (PBPs). This results in the interruption of cell wall (peptidoglycan) biosynthesis, which leads to bacterial cell lysis and death.

5.2. Pharmacokinetic properties

Absorption

After intravenous infusion and intravenous injection of 1 g of Ceftazidime for Injection, the peak plasma concentrations (Cmax) are achieved to 70-72 mg/L and 120-146 mg/L. The half-life ($t_{1/2\beta}$) of blood drug elimination of Ceftazidime is about 1.5-2.3 hours.

Distribution

The distribution of Ceftazidime is good in bones, heart, bile, sputum, aqueous humor, synovial fluid, pleural fluid and peritoneal fluid. Ceftazidime crosses the placenta readily. Penetration of the intact blood-brain barrier is poor. The drug concentration in brain spinal fluid is up to 17%-30% of blood drug concentration when meningitis is occurred. The degree of protein binding with blood serum is about 5%-23%.

Biotransformation

Ceftazidime is not metabolised.

Elimination

Ceftazidime is excreted unchanged into the urine by glomerular filtration; approximately 84 to 87 % of the dose is recovered in the urine within 24 h. Less than 1 % is excreted via the bile.

The half-life of ceftazidime for patients with moderate and severe renal impairments is prolonged. The half-life is prolonged to 14 to 30 hours when the endogenous creatinine clearance rate is less than 2 mL/min. The half-life for Neonates is prolonged to 4-5 hours. Ceftazidime can be eliminated by hematodialysis.

5.3. Preclinical safety data

Non-clinical data reveal no special hazard for humans based on studies of safety pharmacology, repeat dose toxicity, genotoxicity, toxicity to reproduction. Carcinogenicity studies have not been performed with ceftazidime.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Sodium carbonate (anhydrous sterile)

6.2. Incompatibilities

Ceftazidime for Injection is less stable in Sodium Bicarbonate Injection than in other intravenous fluids. It is not recommended as a diluent. Ceftazidime for Injection and aminoglycosides should not be mixed in the same giving set or syringe. Precipitation has been reported with vancomycin added to ceftazidime in solution. Therefore, it would be prudent to flush giving sets and intravenous lines between administration of these two agents.

6.3. Shelf life

3 years

6.4. Special precautions for storage

Preserve in a tight container, store below 30°C and protect from light.

6.5. Nature and contents of container

Ceftazidime powders for solution for injection or infusion is packaged in a 10-mL injection vials made of soda-lime glass with a halogenated butyl rubber stopper and an aluminum-plastic combination caps for antibiotic vials.

6.6. Instructions for use and handling

As the product dissolves, carbon dioxide is released and a positive pressure develops. Small bubbles of carbon dioxide in the constituted solution may be ignored.

Instructions for constitution:

Add 10 mL of Water for Injection to the vials and dilute completely. Administer by slow intravenous injection after 3-5 minutes after completely dissolution.

Dilute above solution with 100 mL of 5% glucose solution or saline solution, then administer by intravenous infusion in 20-30 minutes.

7. MARKETING AUTHORISATION HOLDER

Shandong Luoxin Pharmaceutical Group Stock Co., Ltd.

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8. NUMBER(S) IN THE NATIONAL REGISTER OF FINISHED PHARMACEUTICAL PRODUCTS

08065/08025/NMR/2019

9. DATE OF FIRST AUTHORISATION/RENEWALOF THE AUTHORISATION

Mar 19, 2023

10. DATE OF REVISION OF THE TEXT