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Rx only

## **CEFTAZIDIME-ZHIJUN Powder for Injection**

Ceftazidime for Injection

### **NAME OF THE PRODUCT**

Trade name: CEFTAZIDIME-ZHIJUN 500mg Powder for Injection and CEFTAZIDIME-ZHIJUN 1g Powder for Injection

Generic Name: Ceftazidime for Injection 500mg and Ceftazidime for Injection 1g

### **NAME AND STRENGTH OF ACTIVE INGREDIENTS**

#### CEFTAZIDIME-ZHIJUN 500mg Powder for Injection

Active Ingredients: Ceftazidime pentahydrate

Strength: Equivalent to 500g of ceftazidime

#### CEFTAZIDIME-ZHIJUN 1g Powder for Injection

Active Ingredients: Ceftazidime pentahydrate

Strength: Equivalent to 1g of ceftazidime

### **DOSAGE FORM**

Powder for injection

### **DESCRIPTION**

Ceftazidime is a white to slightly yellow powder. Each vial of CEFTAZIDIME-ZHIJUN 500mg/1.0g Powder for Injection contains 500mg/1.0g of ceftazidime as ceftazidime pentahydrate and 59mg/118mg of sodium carbonate. Reconstituted solutions of CEFTAZIDIME-ZHIJUN 500mg/1.0g Powder for Injection range in color from light yellow to amber, depending on the diluent and volume used.

### **For CEFTAZIDIME-ZHIJUN 500g Powder for Injection and CEFTAZIDIME-ZHIJUN 1g Powder for Injection**

CEFTAZIDIME-ZHIJUN may be constituted for IM use with 0.5% or 1% lignocaine HCl injection, or constituted with water for injection for IM use.

For IV injection use it should be constituted with water for injection.

**FOR CEFTAZIDIME-ZHIJUN 1g Powder for Injection only** It also can be reconstituted for IV infusion with following diluents: 0.9% Sodium chloride injection; M/6 sodium lactate injection; compound sodium lactate injection (Hartmann's solution); 5% dextrose injection; 0.225% sodium



chloride and 5% dextrose injection; 0.45% sodium chloride and 5% dextrose injection; 0.9% sodium chloride and 5% dextrose injection; 0.18% sodium chloride and 4% dextrose injection; 10% dextrose injection; Dextran 40 injection 10% in 0.9% sodium chloride injection; Dextran 40 injection 10% in 5% dextrose injection; Dextran 70 injection 6% in 0.9% sodium chloride injection; Dextran 70 injection 6% in 5% dextrose injection.

The solutions for IV injection or infusion, and IM injection can be prepared by introducing appropriate amount of diluents.

The solutions for IV injection or infusion, and IM injection can be prepared by introducing appropriate amount of diluents. Please see **Route of Administration** for the detailed solution preparation method.

## PHARMACODYNAMICS

Ceftazidime is bactericidal in action. It acts by inhibiting bacterial cell wall synthesis.

**Microbiology:** A wide range of pathogenic strains and isolates are susceptible in vitro, including strains resistant to gentamicin and other aminoglycosides. Ceftazidime is highly stable to most clinically important  $\beta$ -lactamases produced by both gram-positive and gram-negative organisms, therefore it is active against many ampicillin- and cephalothin-resistant strains. Ceftazidime has high intrinsic activity in vitro and acts within a narrow MIC range for most genera with minimal changes in MIC at varied inoculum levels. In vitro, the activities of ceftazidime and aminoglycosides in combination are additive. There is evidence of synergy in some strains.

Ceftazidime is active in vitro against the following organisms:

**Gram-Negative:** *Pseudomonas aeruginosa*, *Pseudomonas spp.* (including *Ps. pseudomallei*), *Escherichia coli*, *Klebsiella spp.* (including *Klebsiella pneumoniae*), *Proteus mirabilis*, *Proteus vulgaris*, *Morganella morganii* (formerly *Proteus morganii*), *Proteus rettgeri*, *Providencia*, *Enterobacter*, *Citrobacter*, *Serratia*, *Salmonella* and *Shigella spp.*, *Pasteurella multocida*, *Yersinia enterocolitica*, *Acinetobacter spp.*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Haemophilus influenzae* (including ampicillin-resistant strains), *Haemophilus parainfluenzae* (including ampicillin-resistant strains).

**Gram-Positive:** *Staphylococcus aureus* (methicillin-sensitive strains), *Staphylococcus epidermidis* (methicillin-sensitive strains), *Micrococcus spp.*, *Streptococcus pyogenes* (Group A  $\beta$ -hemolytic *Streptococci*), *Streptococcus Group B* (*S. agalactiae*), *Streptococcus pneumoniae*, *Streptococcus mitis*, *Streptococcus spp.* [excluding *Enterococcus (Streptococcus faecalis)*].

**Anaerobic Strains:** *Peptococcus*, *Peptostreptococcus*, *Streptococcus* and *Propionibacterium spp.*, *Clostridium perfringens*, *Fusobacterium spp.*, *Bacteroides spp.* (many strains of *Bacteroides fragilis* are resistant).

Ceftazidime is not active in vitro against the following organisms: Methicillin-resistant *Staphylococci*, *Enterococcus (Streptococcus faecalis)* and many other *Enterococci*, *Clostridium*

*difficile, Listeria monocytogenes, Campylobacter spp.*

## PHARMACOKINETICS

### **Absorption:**

After intramuscular administration of 500 mg and 1 g of ceftazidime, peak plasma levels of 18 and 37 mg/L respectively are achieved rapidly. Five minutes after intravenous bolus injection of 500 mg, 1 g or 2 g, plasma levels are 46, 87 and 170 mg/L, respectively. The kinetics of ceftazidime are linear within the single dose range of 0.5g to 2g following intravenous or intramuscular dosing.

### **Distribution:**

The serum protein binding of ceftazidime is low at about 10%. Concentrations in excess of the MIC for common pathogens can be achieved in tissues such as bone, heart, bile, sputum, aqueous humour, synovial, pleural and peritoneal fluids. Ceftazidime crosses the placenta readily, and is excreted in the breast milk. Penetration of the intact blood-brain barrier is poor, resulting in low levels of ceftazidime in the CSF in the absence of inflammation. However, concentrations of 4 to 20 mg/l or more are achieved in the CSF when the meninges are inflamed.

### **Biotransformation:**

Ceftazidime is not metabolized.

### **Elimination:**

After parenteral administration plasma levels decrease with a half-life of about 2 h. Ceftazidime is excreted unchanged into the urine by glomerular filtration; approximately 80 to 90 % of the dose is recovered in the urine within 24 h. Less than 1 % is excreted via the bile.

### **Special Patient Populations:**

#### Renal impairment

Elimination of ceftazidime is decreased in patients with impaired renal function and the dose should be reduced (see section **RECOMMENDED DOSAGE**).

#### Hepatic impairment

The presence of mild to moderate hepatic dysfunction had no effect on the pharmacokinetics of ceftazidime in individuals administered 2 g intravenously every 8 hours for 5 days, provided renal function was not impaired (see section **RECOMMENDED DOSAGE**).

#### Elderly

The reduced clearance observed in elderly patients was primarily due to age-related decrease in renal clearance of ceftazidime. The mean elimination half-life ranged from 3.5 to 4 hours following single or 7 days repeat BID dosing of 2 g IV bolus injections in elderly patients 80 years or older.

#### Paediatric population

The half-life of ceftazidime is prolonged in preterm and term neonates by 4.5 to 7.5 hours after

doses of 25 to 30 mg/kg. However, by the age of 2 months the half-life is within the range for adults.

## INDICATIONS

Treatment of single or multiple infections caused by susceptible organisms.

May be used alone as first choice drug before the results of sensitivity tests are available.

May be used in combination with an aminoglycoside or most other beta-lactam antibiotics.

May be used with an antibiotic against anaerobes when the presence of *Bacteroides fragilis* is suspected.

Susceptibility to ceftazidime will vary with geography and time and local susceptibility data should be consulted where available.

### Indications include:

- severe infections e.g.      - septicaemia, bacteraemia, peritonitis, meningitis.
- infections in immunosuppressed patients
- infections in patients in intensive care, e.g. infected burns
- respiratory tract infections including lung infections in cystic fibrosis
- ear, nose and throat infections
- urinary tract infections
- skin and soft tissue infections
- gastrointestinal, biliary and abdominal infections
- bone and joint infections
- infections associated with haemo- and peritoneal dialysis and with continuous ambulatory peritoneal dialysis (CAPD).

## RECOMMENDED DOSAGE

Dosage depends upon the severity, sensitivity, site and type of infection and upon the age, and renal function of the patient.

CEFTAZIDIME-ZHIJUN 1.0g Powder for Injection may be administered by IV injection or infusion or by deep IM injection.

CEFTAZIDIME-ZHIJUN 500mg Powder for Injection may be administered by IV injection or by deep IM injection.

Recommended IM injection sites are the upper outer quadrant of the gluteus maximus or lateral part of the thigh.

CEFTAZIDIME-ZHIJUN solutions may be given directly into the vein or introduced into the tubing of a giving set if the patient is receiving parenteral fluids.

### Adults

1 to 6 g/day in two or three divided doses by i.v. or i.m. injection.

Urinary tract and less severe infections: 500 mg or 1 g every 12 h.

Most infections: 1 g every 8 h or 2 g every 12 h.

Very severe infections particularly in immunocompromised patients including those with neutropenia: 2 g every eight or 12 h, or 3 g every 12 h.

Fibrocystic adults with pseudomonal lung infections: 100 to 150 mg/kg/day in three divided doses.

In adults with normal renal function 9 g/day has been used without ill effect.

### **Infants and children (greater than 2 months)**

30 to 100 mg/kg/day in two or three divided doses.

Doses up to 150 mg/kg/day (maximum 6 g/day) in three divided doses may be given to infected immunocompromised or fibrocystic children or children with meningitis.

### **Neonates (0 to 2 months)**

25 to 60 mg/kg/day in two divided doses.

In neonates, the serum half life of ceftazidime can be three to four times that in adults.

### **Elderly**

In view of the reduced clearance of ceftazidime in acutely ill elderly patients, the daily dosage should not normally exceed 3 g, especially in those over 80 years of age.

### **Renal Impairment**

Ceftazidime is excreted unchanged by the kidneys. Therefore, in patients with impaired renal function, the dosage should be reduced. An initial loading dose of 1 g should be given. Maintenance doses should be based on creatinine clearance:

#### **Recommended maintenance doses of *CEFTAZIDIME-ZHIJUN* in renal insufficiency:**

| Creatinine Clearance<br>(ml / min) | Approx. Serum creatinine<br>(micromoles / l) (mg / dl) | Recommended unit dose of<br><i>CEFTAZIDIME-ZHIJUN</i> (g) | Frequency of<br>dosing (hourly) |
|------------------------------------|--------------------------------------------------------|-----------------------------------------------------------|---------------------------------|
| 50                                 | 150 ( <1.7 )                                           | Normal dosage                                             |                                 |
| 50 – 31                            | 150 – 200 ( 1.7 - 2.3 )                                | 1.0                                                       | 12                              |
| 30 – 16                            | 200 – 350 ( 2.3 - 4.0 )                                | 1.0                                                       | 24                              |
| 15 – 6                             | 350 – 500 ( 4.0 - 5.6 )                                | 0.5                                                       | 24                              |
| 5                                  | 500 ( 5.6 )                                            | 0.5                                                       | 48                              |

In patients with severe infections the unit dose should be increased by 50% or the dosing frequency increased. In such patients the ceftazidime serum levels should be monitored and trough levels should not exceed 40 mg/l.

In children the creatinine clearance should be adjusted for body surface area or lean body mass.

### **Haemodialysis**

The serum half-life during haemodialysis ranges from 3 to 5 h.

Following each haemodialysis period, the maintenance dose of *CEFTAZIDIME-ZHIJUN* recommended in the above table should be repeated.

### Peritoneal dialysis

*CEFTAZIDIME-ZHIJUN* may be used in peritoneal dialysis and continuous ambulatory peritoneal dialysis (CAPD).

In addition to IV use, *CEFTAZIDIME-ZHIJUN* can be incorporated into the dialysis fluid (usually 125 to 250 mg for 2 litres of dialysis solution).

For patients in renal failure on continuous arteriovenous haemodialysis or high-flux haemofiltration in intensive therapy units; 1 g daily either as a single dose or in divided doses. For low-flux haemofiltration, follow the dosage recommended under impaired renal function.

For patients on venovenous haemofiltration and venovenous haemodialysis, follow the dosage recommendations in the tables below.

### Continuous venovenous haemofiltration dosage guidelines for *CEFTAZIDIME-ZHIJUN*

| Residual renal function<br>(creatinine clearance in ml/min) | Maintenance dose (mg) for a ultrafiltration rate (ml/min) of <sup>a</sup> : |      |      |     |
|-------------------------------------------------------------|-----------------------------------------------------------------------------|------|------|-----|
|                                                             | 5                                                                           | 16.7 | 33.3 | 50  |
| 0                                                           | 250                                                                         | 250  | 500  | 500 |
| 5                                                           | 250                                                                         | 250  | 500  | 500 |
| 10                                                          | 250                                                                         | 500  | 500  | 750 |
| 15                                                          | 250                                                                         | 500  | 500  | 750 |
| 20                                                          | 500                                                                         | 500  | 500  | 750 |

<sup>a</sup>- Maintenance dose to be administered every 12 h.

### *CEFTAZIDIME-ZHIJUN* dosage guidelines during continuous venovenous haemodialysis

| Residual renal function (creatinine clearance in ml/min) | Maintenance dose (mg) for a dialysate in flow rate of <sup>a</sup> : |     |      |                                 |     |      |
|----------------------------------------------------------|----------------------------------------------------------------------|-----|------|---------------------------------|-----|------|
|                                                          | 1.0 litre/h                                                          |     |      | 2.0 litres/h                    |     |      |
|                                                          | Ultrafiltration rate (litre/h)                                       |     |      | Ultrafiltration rate (litres/h) |     |      |
|                                                          | 0.5                                                                  | 1.0 | 2.0  | 0.5                             | 1.0 | 2.0  |
| 0                                                        | 500                                                                  | 500 | 500  | 500                             | 500 | 750  |
| 5                                                        | 500                                                                  | 500 | 750  | 500                             | 500 | 750  |
| 10                                                       | 500                                                                  | 500 | 750  | 500                             | 750 | 1000 |
| 15                                                       | 500                                                                  | 750 | 750  | 750                             | 750 | 1000 |
| 20                                                       | 750                                                                  | 750 | 1000 | 750                             |     |      |

### **ROUTE OF ADMINISTRATION**

*CEFTAZIDIME-ZHIJUN* 1g Powder for Injection may be administered by IV injection or infusion,

or by deep IM injection.

CEFTAZIDIME-ZHIJUN 500mg Powder for Injection may be administered by IV injection or by deep IM injection.

Recommended IM injection sites are the upper outer quadrant of the gluteus maximus or lateral part of the thigh.

CEFTAZIDIME-ZHIJUN solutions may be given directly into the vein or introduced into the tubing of a giving set if the patient is receiving parenteral fluids.

CEFTAZIDIME-ZHIJUN is compatible with most commonly used IV fluids. However, sodium bicarbonate injection is not recommended as diluent (see **Incompatibilities** under **INTERACTIONS WITH OTHER MEDICATIONS**).

**Table 4 Preparation of Solution**

| Vial Size |             | Amount of Diluent to be added<br>(mL) | Approximate Concentration<br>(mg/mL) |
|-----------|-------------|---------------------------------------|--------------------------------------|
| 500mg     | IM          | 1.5                                   | 260                                  |
|           | IV bolus    | 5                                     | 90                                   |
| 1.0g      | IM          | 3                                     | 260                                  |
|           | IV bolus    | 10                                    | 90                                   |
|           | IV infusion | 50 <sup>★</sup>                       | 20                                   |

★ note: Addition should be in 2 stages (see text)

Solutions range from light yellow to amber depending on concentration, diluent and storage conditions used. Within the stated recommendations, product potency is not adversely affected by such colour variations. Ceftazidime at concentrations between 1 and 40 mg/mL is compatible with: 0.9% Sodium chloride injection; M/6 sodium lactate injection; compound sodium lactate injection (Hartmann's solution); 5% dextrose injection; 0.225% sodium chloride and 5% dextrose injection; 0.45% sodium chloride and 5% dextrose injection; 0.9% sodium chloride and 5% dextrose injection; 0.18% sodium chloride and 4% dextrose injection; 10% dextrose injection; Dextran 40 injection 10% in 0.9% sodium chloride injection; Dextran 40 injection 10% in 5% dextrose injection; Dextran 70 injection 6% in 0.9% sodium chloride injection; Dextran 70 injection 6% in 5% dextrose injection. Ceftazidime at concentrations between 0.05 and 0.25 mg/mL is compatible with intraperitoneal dialysis fluid (lactate). CEFTAZIDIME-ZHIJUN may be constituted for IM use with 0.5% or 1% lignocaine HCl injection.

Both components retain satisfactory potency when ceftazidime at 4 mg/mL is admixed with: Hydrocortisone (hydrocortisone sodium phosphate) 1 mg/mL in 0.9% sodium chloride injection or 5% dextrose injection; cefuroxime (cefuroxime sodium) 3 mg/mL in 0.9% sodium chloride injection; cloxacillin (cloxacillin sodium) 4 mg/mL in 0.9% sodium chloride injection; heparin 10 or 50 iu/mL in 0.9% sodium chloride injection; potassium chloride 10 or 40 mEq/L in 0.9% sodium

chloride injection.

The contents of a 500-mg vial of CEFTAZIDIME-ZHIJUN, constituted with 1.5 mL water for injections, may be added to metronidazole injection (500 mg in 100 mL) and both retain their activity.

**Preparation of Solutions for IM or IV Bolus Injection:** Introduce the syringe needle through the vial closure and inject the recommended volume of diluent. Withdraw the needle and shake the vial to give a clear solution. Invert the vial. With the syringe piston fully depressed, insert the needle into the solution. Withdraw the total volume of solution into the syringe ensuring that the needle remains in the solution. Small bubbles may be disregarded.

**Preparation of Solutions for IV Infusion from 1g vials:** Prepare using a total of 50 mL (for 1 g vials) of compatible diluent, added in 2 stages as follows:

1g vials for IV infusion: Introduce the syringe needle through the vial closure and inject 10 ml of diluent. Withdraw the needle and shake the vial to give a clear solution. Do not insert a gas relief needle until the product has dissolved. Insert a gas relief needle through the vial closure to relieve the internal pressure. Transfer the reconstituted solution to final delivery vehicle making up a total volume of at least 50 mL, and administer by IV infusion over 15-30 min.

Note: To preserve product sterility, it is important that the gas relief needle is not inserted through the vial closure before the product has dissolved

## CONTRAINDICATION

Hypersensitivity to ceftazidime, to any other cephalosporin or to any of the excipients.

History of severe hypersensitivity (e.g. anaphylactic reaction) to any other type of beta-lactam antibacterial agent (penicillins, monobactams and carbapenems).

## WARNING AND PRECAUTIONS

Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients receiving therapy with beta-lactams.

Before initiating therapy with CEFTAZIDIME-ZHIJUN, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, carbapenems or other beta-lactam agents. If an allergic reaction occurs, CEFTAZIDIME-ZHIJUN must be discontinued immediately and appropriate alternative therapy instituted.

As with all beta-lactam antibacterial agents, serious and occasionally fatal hypersensitivity reactions have been reported. In case of severe hypersensitivity reactions, treatment with ceftazidime must be discontinued immediately and adequate emergency measures must be initiated.

Before beginning treatment, it should be established whether the patient has a history of severe hypersensitivity reactions to ceftazidime, to other cephalosporins or to any other type of beta-lactam agent. Caution should be used if ceftazidime is given to patients with a history of non-severe hypersensitivity to other beta-lactam agents.



Ceftazidime has a limited spectrum of antibacterial activity. It is not suitable for use as a single agent for the treatment of some types of infections unless the pathogen is already documented and known to be susceptible or there is a very high suspicion that the most likely pathogen(s) would be suitable for treatment with ceftazidime. This particularly applies when considering the treatment of patients with bacteraemia and when treating bacterial meningitis, skin and soft tissue infections and bone and joint infections. In addition, ceftazidime is susceptible to hydrolysis by several of the extended spectrum beta lactamases (ESBLs). Therefore information on the prevalence of ESBL producing organisms should be taken into account when selecting ceftazidime for treatment.

Antibacterial agent-associated colitis and pseudo-membranous colitis have been reported with nearly all anti-bacterial agents, including ceftazidime, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea during or subsequent to the administration of ceftazidime. Discontinuation of therapy with ceftazidime and the administration of specific treatment for *Clostridium difficile* should be considered. Medicinal products that inhibit peristalsis should not be given.

Concurrent treatment with high doses of cephalosporins and nephrotoxic medicinal products such as aminoglycosides or potent diuretics (e.g. furosemide) may adversely affect renal function.

Ceftazidime is eliminated via the kidneys, therefore the dose should be reduced according to the degree of renal impairment. Patients with renal impairment should be closely monitored for both safety and efficacy. Neurological sequelae have occasionally been reported when the dose has not been reduced in patients with renal impairment.

Prolonged use may result in the overgrowth of non-susceptible organisms (e.g. Enterococci, fungi) which may require interruption of treatment or other appropriate measures. Repeated evaluation of the patient's condition is essential.

Ceftazidime does not interfere with enzyme-based tests for glycosuria, but slight interference (false-positive) may occur with copper reduction methods (Benedict's, Fehling's, Clinitest).

Ceftazidime does not interfere in the alkaline picrate assay for creatinine.

The development of a positive Coombs' test associated with the use of ceftazidime in about 5% of patients may interfere with the cross-matching of blood.

Important information about one of the ingredients of CEFTAZIDIME-ZHIJUN 500mg/1.0g

Powder for Injection:

CEFTAZIDIME-ZHIJUN 500mg Powder for Injection contains 26 mg of sodium per vial.

CEFTAZIDIME-ZHIJIN 1.0g Powder for Injection contains 52mg of sodium per vial.

This should be considered for patients who are on a controlled sodium diet.

## **INTERACTIONS WITH OTHER MEDICATIONS**

Interaction studies have only been conducted with a probenecid and furosemide.

Concurrent use of high doses with nephrotoxic medicinal products may adversely affect renal function.

Chloramphenicol is antagonistic *in vitro* with ceftazidime and other cephalosporins. The clinical relevance of this finding is unknown, but if concurrent administration of ceftazidime with chloramphenicol is proposed, the possibility of antagonism should be considered.

**Incompatibilities:** Ceftazidime is less stable in Sodium Bicarbonate Injection than other intravenous fluids. It is not recommended as a diluent.

Ceftazidime and aminoglycosides should not be mixed in the same giving set or syringe. Precipitation has been reported when vancomycin has been added to ceftazidime in solution. It is recommended that giving sets and intravenous lines are flushed between administration of these two agents.

## PREGNANCY AND LACTATION

### Pregnancy

There are limited amounts of data from the use of ceftazidime in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.

CEFTAZIDIME-ZHIJUN should be prescribed to pregnant women only if the benefit outweighs the risk.

### Breast-feeding

Ceftazidime is excreted in human milk in small quantities but at therapeutic doses of ceftazidime no effects on the breast-fed infant are anticipated. Ceftazidime can be used during breast-feeding.

## SIDE EFFECTS

The most common adverse reactions are eosinophilia, thrombocytosis, phlebitis or thrombophlebitis with intravenous administration, diarrhoea, transient increases in hepatic enzymes, maculopapular or urticarial rash, pain and/or inflammation following intramuscular injection and positive Coomb's test.

Data from sponsored and unsponsored clinical trials have been used to determine the frequency of common and uncommon undesirable effects. The frequencies assigned to all other undesirable effects were mainly determined using post-marketing data and refer to a reporting rate rather than a true frequency. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness. The following convention has been used for the classification of frequency:

| <u>System Organ Class</u>          | <u>Common</u> | <u>Uncommon</u>                                   | <u>Very rare</u> | <u>Unknown</u> |
|------------------------------------|---------------|---------------------------------------------------|------------------|----------------|
| <u>Infections and infestations</u> |               | Candidiasis (including vaginitis and oral thrush) |                  |                |

|                                               |                                                                  |                                                                                                                                                  |                        |                                                                                                   |
|-----------------------------------------------|------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|---------------------------------------------------------------------------------------------------|
| <u>Blood and lymphatic system disorders</u>   | Eosinophilia<br>Thrombocytosis                                   | Neutropenia<br>Leucopenia<br>Thrombocytopenia                                                                                                    |                        | Agranulocytosis<br>Haemolytic anaemia<br>Lymphocytosis                                            |
| <u>Immune system disorders</u>                |                                                                  |                                                                                                                                                  |                        | Anaphylaxis<br>(including bronchospasm and/or hypotension) (see <b>Warnings and Precautions</b> ) |
| <u>Nervous system disorders</u>               |                                                                  | Headache<br>Dizziness                                                                                                                            |                        | Neurological sequelae <sup>1</sup><br>Paraesthesia                                                |
| <u>Vascular disorders</u>                     | Phlebitis or thrombophlebitis with intravenous administration    |                                                                                                                                                  |                        |                                                                                                   |
| <u>Gastrointestinal disorders</u>             | Diarrhoea                                                        | Antibacterial agent-associated diarrhoea and colitis <sup>2</sup> (see <b>Warnings and Precautions</b> )<br>Abdominal pain<br>Nausea<br>Vomiting |                        | Bad taste                                                                                         |
| <u>Heptobiliary disorders</u>                 | Transient elevations in one or more hepatic enzymes <sup>3</sup> |                                                                                                                                                  |                        | Jaundice                                                                                          |
| <u>Skin and subcutaneous tissue disorders</u> | Maculopapular or urticarial rash                                 | Pruritus                                                                                                                                         |                        | Toxic epidermal necrolysis<br>Stevens-Johnson syndrome<br>Erythema multiforme<br>Angioedema       |
| <u>Renal and urinary disorders</u>            |                                                                  | Transient elevations of blood urea, blood urea                                                                                                   | Interstitial nephritis |                                                                                                   |

|                                                             |                                                        |                                  |                     |  |
|-------------------------------------------------------------|--------------------------------------------------------|----------------------------------|---------------------|--|
|                                                             |                                                        | nitrogen and/or serum creatinine | Acute renal failure |  |
| <u>General disorders and administration site conditions</u> | Pain and/or inflammation after intramuscular injection | Fever                            |                     |  |
| <u>Investigations</u>                                       | Positive Coombs' test <sup>4</sup>                     |                                  |                     |  |

<sup>1</sup>There have been reports of neurological sequelae including tremor, myoclonia, convulsions, encephalopathy and coma in patients with renal impairment in whom the dose has not been appropriately reduced.

<sup>2</sup>Diarrhoea and colitis may be associated with *Clostridium difficile* and may present as pseudomembranous colitis.

<sup>3</sup>ALT (SGPT), AST (SOGT), LHD, GGT, alkaline phosphatase.

<sup>4</sup>A positive Coombs test develops in about 5% of patients and may interfere with blood cross matching.

## OVERDOSAGE

Overdosage can lead to neurological sequelae including encephalopathy, convulsions and coma. Serum levels of ceftazidime can be reduced by haemodialysis or peritoneal dialysis.

## STORAGE CONDITION

Dry powder: Store below 30 °C and protect from light.

Reconstituted solutions:

CEFTAZIDIME-ZHIJUN 1g Powder for Injection: Reconstituted solutions for IM injection and IV injection or infusion retain their physical and chemical stability for 4 hrs below 25 °C or 24 hrs in the refrigerator (2-8 °C).

CEFTAZIDIME-ZHIJUN 500mg Powder for Injection: Reconstituted solutions for IM injection and IV injection retain their physical and chemical stability for 4 hrs below 25 °C or 24 hrs in the refrigerator (2-8 °C).

## SHELF LIFE

Dry powder: 24 months

Reconstituted solutions:

CEFTAZIDIME-ZHIJUN 1g Powder for Injection: Reconstituted solutions for IM injection and IV injection or infusion retain their physical and chemical stability for 4 hrs below 25 °C or 24 hrs in

the refrigerator (2-8 ℃).

CEFTAZIDIME-ZHIJUN 500mg Powder for Injection: Reconstituted solutions for IM injection and IV injection retain their physical and chemical stability for 4 hrs below 25 ℃ or 24 hrs in the refrigerator (2-8 ℃).



**Manufacturer:**

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