AUSTRALIAN PRODUCT INFORMATION

CEFTAZIDIME VIATRIS

(ceftazidime pentahydrate) powder for injection

1 NAME OF THE MEDICINE

Ceftazidime pentahydrate

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

CEFTAZIDIME VIATRIS is supplied in vials containing 1 g and 2 g of ceftazidime (as pentahydrate).

116.4 mg ceftazidime pentahydrate is equivalent to 100 mg ceftazidime free acid.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

CEFTAZIDIME VIATRIS is a powder for injection and is a white or almost white, crystalline powder.

On the addition of water for injections, CEFTAZIDIME VIATRIS dissolves with effervescence to produce a solution for injection.

CEFTAZIDIME VIATRIS containing 1 g ceftazidime (as pentahydrate) is used for IV injection or IM injection.

CEFTAZIDIME VIATRIS containing 2 g ceftazidime (as pentahydrate) is used for IV injection or IV infusion.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

CEFTAZIDIME VIATRIS is indicated for the treatment of single and mixed infections caused by susceptible aerobic organisms with suspected or documented resistance to other antimicrobials, but not to ceftazidime, and as an alternative to aminoglycosides in pseudomonal infection in patients in whom aminoglycoside toxicity is a cause for concern and other pseudomonal antibiotics cannot be used.

Indications include:

Severe infections in general: for example septicaemia, including neonatal sepsis, bacteraemia, and in patients in intensive care units with specific problems, e.g., infected burns.

Respiratory tract infections: for example, pneumonia, broncho-pneumonia, infected pleurisy, infected bronchiectasis and bronchitis.

Severe ear, nose and throat infections: for example, otitis media, mastoiditis.

Urinary tract infections: for example, acute and chronic pyelonephritis, pyelitis, cystitis, urethritis (bacterial only), and infections associated with bladder and renal stones.

Skin and soft tissue infections: for example, erysipelas, abscesses, cellulitis, infected burns and wounds, mastitis.

Gastrointestinal and abdominal infections: for example, intra-abdominal abscesses, enterocolitis.

Bone and joint infections: for example, osteitis, osteomyelitis, septic arthritis, infected bursitis.

4.2 DOSE AND METHOD OF ADMINISTRATION

Note: Vials of CEFTAZIDIME VIATRIS as supplied are under reduced pressure; a positive pressure is produced on reconstitution due to the release of carbon dioxide.

General dosage recommendations

Ceftazidime is to be used by the parenteral route, the dosage depending upon the severity, sensitivity and type of infection and the age, weight and renal function of the patient.

Adults

The adult dosage range for ceftazidime is 1 to 6 g per day: for instance, 500 mg, 1 g or 2 g given 12 or 8 hourly by I.V. or I.M. injection. In urinary tract infections and in many less serious infections, 500 mg or 1 g 12 hourly is usually adequate. In the majority of infections, 1 g 8 hourly or 2 g 12 hourly should be given. In very severe infections, 2 g 8 or 12 hourly should be administered. Individual doses exceeding 1 g should be administered intravenously.

Children

The usual dosage range for children aged over 12 months is 25 to 100 mg/kg/day (up to a maximum of 6 g/day) given as two or three divided doses. The maximum daily dosage (6 g) may be given to children with very serious infections e.g. those who are immunocompromised or who suffer from cystic fibrosis.

Neonates and infants up to 12 months

25-100 mg/kg/day in two divided doses. In neonates the serum half-life of ceftazidime can be 3-4 times greater than that measured in adults.

Use in the elderly

In view of the reduced clearance of ceftazidime in elderly patients, the daily dosage should be adjusted according to renal function.

Dosage in Impaired Renal Function

Ceftazidime is excreted by the kidneys almost exclusively by glomerular filtration. Therefore, in patients with impaired renal function it is recommended that the dosage of ceftazidime should be reduced to compensate for its slower excretion, except in mild impairment, ie glomerular filtration rate (GFR) greater than 50 mL/min. In patients with suspected renal insufficiency, an initial loading dose of 1 g of ceftazidime may be given. An estimate of GFR should be made to determine the appropriate maintenance dose.

Recommended maintenance doses are shown below:

Table 1. Recommended maintenance doses of ceftazidime in renal insufficiency

Creatinine clearance mL/min	Approx. Serum creatinine # micromol/L	Recommended Unit dose of ceftazidime	Frequency of dosing Hourly
50-31	150-200	1.0	12
30-16	200-350	1.0	24
15-6	350-500	0.5	24
5	500	0.5	48

These values are guidelines and may not accurately predict renal function in all patients especially in the elderly in whom the serum creatinine concentration may overestimate renal function.

In patients with severe infections who would normally receive 6 g of ceftazidime daily were it not for renal insufficiency, the unit dose given in the table above may be increased by 50% or the dosing frequency increased appropriately. In such patients it is recommended that ceftazidime serum levels should be monitored and trough levels should not exceed 40 mg/L.

When only serum creatinine is available, the following formula (Cockcroft's equation) may be used to estimate creatinine clearance. The serum creatinine should represent a steady state of renal function:

Males:

$$\text{Creatinine clearance (mL/min)} = \frac{\text{Weight (kg) x (140 − age in years) x 88.4}}{\text{72 x serum creatinine (micromol/L)}}$$

Females:

0.85 × above value.

In children the creatinine clearance should be adjusted for body surface area or lean body mass and the dosing frequency reduced in cases of renal insufficiency as for adults.

The serum half-life of ceftazidime during haemodialysis is approximately 3 hours. The appropriate maintenance dose of ceftazidime should be repeated following each haemodialysis period. Continuous ambulatory peritoneal dialysis (CAPD) removed approximately 10% of the antibiotic when the dwell time was 4-6 hours.

Administration

Ceftazidime may be given intravenously or by deep intramuscular injection into a large muscle mass such as the upper outer quadrant of the gluteus maximus or lateral part of the thigh.

Instructions for reconstitution

CEFTAZIDIME VIATRIS may be reconstituted with Water for Injections or, for intramuscular injection, with 1.0% or 0.5% Lidocaine (lignocaine). See *table for addition volumes and solution concentrations*.

To reduce microbiological hazard, use as soon as practicable after reconstitution. If storage is necessary, hold at 2 to 8°C for not more than 24 hours. Protect from light.

Following reconstitution, use in one patient on one occasion only and discard any residue.

Table 2. Preparation of Solution

Preparation of Solution		
Vial size	**Amount of Diluent to be added**	**Approximate Concentration (mg/mL)**
1 g	Intramuscular 3.0 mL	260
	Intravenous 10 mL	90
2 g	intravenous bolus 10 mL	170
	intravenous infusion 50 mL[#]	40

[#]Note: Addition should be in two stages (see text).

All sizes of vials as supplied are under reduced pressure. As the product dissolves carbon dioxide is released and a positive pressure develops. For ease of use, it is recommended that the following techniques of reconstitution are adopted.

1 g I.M./I.V. and 2 g I.V. bolus vials:

1. Insert the syringe needle through the vial closure and inject the recommended volume of diluent. The vacuum may assist entry of the diluent. Remove the syringe needle.

2. Shake to dissolve: carbon dioxide is released and a clear solution obtained in about 1-2 minutes.

3. Invert the vial. With the syringe plunger fully depressed, insert the needle through the vial closure and withdraw the total volume of solution into the syringe (the pressure in the vial may aid withdrawal). Ensure that the needle remains within the solution and does not enter the headspace. The withdrawn solution may contain small bubbles of carbon dioxide; they may be disregarded.

2 g I.V. infusion vial:

This vial may be reconstituted for short intravenous infusion (e.g. up to 30 minutes) as follows:

1. Insert the syringe needle through the vial closure and inject 10 mL of diluent. The vacuum may assist entry of the diluent. Remove the syringe needle.

2. Shake to dissolve; carbon dioxide is released and a clear solution obtained in about 1-2 minutes.

3. Insert a gas relief needle through the vial closure to relieve the internal pressure and, with the gas relief in position, add a further 40 mL of diluent. Remove the gas relief needle and syringe needle; shake the vial and set up for infusion use in the normal way.

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

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

Solutions of CEFTAZIDIME VIATRIS Injection reconstituted in Water for Injections retain satisfactory potency for 12 hours if kept below 25°C or for 7 days if refrigerated (2-8°C). When reconstituted in 0.5% Lidocaine (Lignocaine) Hydrochloride Injection BP the corresponding times are 6 hours at below 25°C or 4 days under refrigeration (2-8°C). Some increase in the colour of prepared solutions of CEFTAZIDIME VIATRIS for injection may occur on storage. It is, however, advisable to use the reconstituted product as soon as possible.

Ceftazidime is compatible with the intravenous fluids shown below. Solutions at concentrations between 1 mg/mL and 40 mg/mL in these infusion fluids may be stored for up to 12 hours below 25°C or 7 days if refrigerated (2-8°C).

- 0.9% Sodium Chloride Injection BP
- M/6 Sodium Lactate Injection BP
- M/6 Compound Sodium Lactate Injection BP (Hartmann's Solution)
- 5% Dextrose Injection BP
- Dextran 40 Injection BP 10% in 0.9% Sodium Chloride Injection BP
- Dextran 40 Injection BP 10% in 5% Dextrose Injection BP
- Dextran 70 Injection BP 6% in 0.9% Sodium Chloride Injection BP

- Dextran 70 Injection BP 6% in 5% Dextrose Injection BP

CEFTAZIDIME VIATRIS Injection may be stored for up to 12 hours below 25°C or 7 days under refrigeration (2-8°C) at concentrations of between 0.05 mg/mL and 0.25 mg/mL in Intraperitoneal Dialysis Fluid (Lactate) BPC 1973.

CEFTAZIDIME VIATRIS Injection has been found compatible for 12 hours below 25°C or 7 days under refrigeration (2- 8°C) when admixed at 4 mg/mL with:

- Potassium Chloride 10 mEq/L or 40 mEq/L in 0.9% Sodium Chloride Injection BP.
- Heparin (10 and 50 units/mL) in 0.9% Sodium Chloride.

CEFTAZIDIME VIATRIS Injection (4 mg/mL) has been found compatible for 24 hours when stored below 25°C or 7 days when refrigerated (2-8°C do not freeze) when admixed with Cloxacillin.

CEFTAZIDIME VIATRIS Injection (5 mg/mL) is compatible for 12 hours when stored below 25°C or 7 days when refrigerated (2-8°C do not freeze) when admixed with metronidazole.

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. Therefore, it would be prudent to flush giving sets and intravenous lines between the administration of these two agents. Protect from light.

CEFTAZIDIME VIATRIS Injection may be reconstituted for intramuscular administration using 0.5% Lidocaine (Lignocaine) Hydrochloride Injection BP; the resultant solutions may be stored for 6 hours below 25°C or 4 days under refrigeration (2-8°C).

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.

Sodium bicarbonate injection is not recommended as a diluent.

Contains no antimicrobial agent. Product is for single use in one patient only. Discard any residue.

4.3 CONTRAINDICATIONS

CEFTAZIDIME VIATRIS is contraindicated in persons who have shown hypersensitivity to cephalosporins or who have experienced a major allergy to penicillin (anaphylaxis, angioneurotic oedema, urticaria).

Lidocaine (lignocaine) should not be used as a diluent for intramuscular injection in patients who are hypersensitive to lidocaine (lignocaine).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Neurotoxicity

There have been reports of neurotoxicity associated with cephalosporin treatment. Symptoms of neurotoxicity include encephalopathy, seizures and/or myoclonus. Risk factors for developing neurotoxicity with cephalosporin treatment include being elderly, renal impairment, central nervous system disorders and intravenous administration. Withdrawal of the medicine should be considered if there are signs of neurotoxicity.

As with other beta-lactam antibiotics, before therapy with ceftazidime is instituted, careful inquiry should be made for a history of hypersensitivity reactions to ceftazidime, cephalosporins, penicillins, or other drugs. Ceftazidime should be given only with special caution to patients with mild type I or immediate

hypersensitivity reactions to penicillin or other beta-lactams. If an allergic reaction to ceftazidime occurs, discontinue the drug. Serious hypersensitivity reactions may require adrenaline (epinephrine), hydrocortisone, antihistamine or other emergency measures.

Antibiotic associated pseudomembranous colitis has been reported with many antibiotics including ceftazidime. A toxin produced by Clostridium difficile appears to be the primary cause. The severity of the colitis may range from mild to life threatening. It is important to consider this diagnosis in patients who develop diarrhoea or colitis in association with antibiotic use (this may occur up to several weeks after cessation of antibiotic therapy). Mild cases usually respond to drug discontinuation alone. However, in moderate to severe cases appropriate therapy with a suitable oral antibacterial agent effective against Clostridium difficile should be considered. Fluids, electrolytes and protein replacement should be provided when indicated. If prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further.

As with other broad spectrum antibiotics, prolonged use may result in the overgrowth of non-susceptible organisms (e.g. Candida enterococci) which may require interruption of treatment or appropriate measures. Repeated evaluation of the patient's condition is essential.

As with other extended-spectrum cephalosporins and penicillins, some initially susceptible strains of Enterobacter spp. and Serratia spp. may develop resistance during ceftazidime therapy. When clinically appropriate during therapy of such infections, periodic susceptibility testing should be considered.

Concurrent treatment with high doses of cephalosporins and nephrotoxic drugs such as aminoglycosides or potent diuretics (e.g. furosemide (frusemide)) may adversely affect renal function. Clinical experience has shown that this is not likely to be a problem with ceftazidime at the recommended dose levels. There is no evidence that ceftazidime adversely affects renal function at normal therapeutic doses.

Drugs which delay peristalsis, e.g. opiates and diphenoxylate with atropine (Lomotil), may prolong and/or worsen the condition and should not be used.

Clostridium difficile infection rarely manifests as diarrhoea in neonates.

Peak concentrations of ceftazidime in the CSF are considerably lower than those in the plasma. Its use in the treatment of infections of the CNS, e.g. meningitis, brain abscess, etc. is not advised at present.

Use in Hepatic Impairment

Transient rises in hepatic enzymes have been noted in some patients given ceftazidime, so careful monitoring of hepatic function is advised when any dysfunction exists.

Repeated use of lidocaine (lignocaine) hydrochloride as a diluent for I.M. use should be avoided in patients with severe liver disease or decreased hepatic blood flow due to the possibility of lidocaine (lignocaine) toxicity resulting from decreased metabolism and consequent accumulation.

As with other broad spectrum antibiotics, prolonged use of ceftazidime may result in the overgrowth of non-susceptible organisms (e.g. Candida, Enterococci) which may require interruption of treatment or adoption of appropriate measures. Repeated evaluation of the patient's condition is essential.

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. There is some evidence in the literature that concurrent use of two beta-lactam antibiotics may exhibit antagonism.

Vials of CEFTAZIDIME VIATRIS as supplied are under reduced pressure; a positive pressure is produced on reconstitution due to the release of carbon dioxide. See Section 4.2 DOSE AND METHOD OF ADMINISTRATION for recommended techniques of reconstitution.

Ceftazidime should be prescribed with caution to individuals with a history of gastrointestinal disease, particularly colitis.

Use in Renal Impairment

Ceftazidime has shown some evidence of renal toxicity in animals. Clinical studies have shown only transient elevations in serum urea and serum creatinine. It is excreted almost entirely by glomerular filtration and its half-life is prolonged in patients with impaired renal function. In such patients dosage adjustment may be required in order to avoid the clinical consequences of elevated antibiotic levels. Neurological sequelae have occasionally been reported when the dose has not been reduced appropriately (see Section 4.2 DOSE AND METHOD OF ADMINISTRATION).

Use in the Elderly

See Section 4.2 DOSE AND METHOD OF ADMINISTRATION**.**

Paediatric Use

Ceftazidime is effective in the treatment of neonatal infections caused by susceptible organisms.

Effects on Laboratory Tests

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.

Ceftazidime does not interfere with enzyme-based tests for glycosuria. Slight interference with copper reduction methods (Benedict's, Fehlings, Clinitest) may be observed. Ceftazidime does not interfere in the alkaline picrate assay for creatinine.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Concurrent use of high doses with nephrotoxic drugs may adversely affect renal function (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

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. There is some evidence in the literature that concurrent use of two beta-lactam antibiotics may exhibit antagonism.

In common with other antibiotics, ceftazidime may affect the gut flora, leading to lower estrogen reabsorption and reduced efficacy of combined oral contraceptives.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on Fertility

No data available.

Use in Pregnancy (Risk Category B1)

The safety of ceftazidime in pregnancy has not been established, although animal studies have not produced evidence of embryopathic or teratogenic effects attributable to ceftazidime. Therefore, it may be administered during known or suspected pregnancy only if in the opinion of the treating physician the expected benefits outweigh the possible risks.

Use in Lactation

Ceftazidime is excreted in human breast milk in low concentrations; therefore, it is not recommended for nursing mothers unless the expected benefits to the mother greatly outweigh any potential risk to the infant.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Data from large clinical trials (internal and published) were used to determine the frequency of very common to 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.

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

very common ≥1/10,

common ≥1/100 to <1/10,

uncommon ≥1/1,000 to <1/100,

rare ≥1/10,000 to <1/1,000,

very rare <1/10,000.

Infections and infestations

Uncommon: Candidiasis (including vaginitis and oral thrush).

Blood and lymphatic system disorders

Common: Eosinophilia and thrombocytosis.

Uncommon: Leucopenia, neutropenia, and thrombocytopenia.

Very rare: Lymphocytosis, haemolytic anaemia, and agranulocytosis.

Immune system disorders

Very rare: Anaphylaxis (including bronchospasm and/or hypotension).

Nervous system disorders

Uncommon: Headache and dizziness

Very rare: Paraesthesia.

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

Vascular disorders

Common: Phlebitis or thrombophlebitis with i.v. administration.

Gastrointestinal disorders

Common: Diarrhoea.

Uncommon: Nausea, vomiting, abdominal pain, and colitis.

Very rare: Bad taste.

As with other cephalosporins, colitis may be associated with Clostridium difficile and may present as pseudomembranous colitis (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

Hepatobiliary disorders

Common: Transient elevations in one or more of the hepatic enzymes, ALT (SGPT), AST (SOGT), LDH, GGT and alkaline phosphatase

Very rare: Jaundice.

Skin and subcutaneous tissue disorders

Common: Maculopapular or urticarial rash.

Uncommon: Pruritus.

Very rare: Angioedema, erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis.

General disorders and administration site conditions

Common: Pain and/or inflammation after i.m. injection.

Uncommon: Fever.

Investigations

Common: Positive Coombs test.

Uncommon: As with some other cephalosporins, transient elevations of blood urea, blood urea nitrogen and/or serum creatinine have been observed.

A positive Coombs test develops in about 5% of patients and may interfere with blood cross-matching.

Reporting Suspected Adverse Effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Overdosage can lead to neurological sequelae including encephalopathy, convulsions and coma. Ceftazidime can be removed by haemodialysis.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of Action

Microbiology

Ceftazidime is bactericidal in action, exerting its effect on target cell wall proteins and causing inhibition of cell wall synthesis. It is stable to most beta-lactamases produced by Gram-positive and Gram-negative organisms and consequently is active against many ampicillin- and cefalothin-resistant strains (but not methicillin-resistant strains). Ceftazidime has been shown to have *in vitro* activity against the following organisms:

Gram-negative:

Pseudomonas aeruginosa

Pseudomonas species (other)

Klebsiella pneumoniae

Klebsiella species (other)

Proteus mirabilis

Proteus vulgaris

Morganella morganii (formerly *Proteus morganii*)

Proteus rettgeri

Providencia species

Escherichia coli

Enterobacter species

Citrobacter species

Serratia species

Acinetobacter species

Neisseria gonorrhoeae

Neisseria meningitidis

Haemophilus influenzae (including ampicillin-resistant strains)

Gram-positive:

Staphylococcus aureus (methicillin-sensitive strains)

Staphylococcus epidermidis (methicillin-sensitive strains)

Micrococcus species

Streptococcus pyogenes

Streptococcus Group B

Streptococcus pneumoniae

Streptococcus species (excluding *Streptococcus faecalis*)

Ceftazidime is not active *in vitro* against methicillin-resistant staphylococci, *Streptococcus faecalis* and many other *Enterococci*, *Listeria monocytogenes*, *Campylobacter* species or *Clostridium difficile*.

In vitro the activities of ceftazidime and aminoglycoside antibiotics in combination have been shown to be at least additive; there is evidence of synergy in some strains tested. This property may be important in the treatment of febrile neutropenic patients.

Susceptibility Tests

Quantitative methods that require measurement of zone diameters give the most precise estimate of antibiotic susceptibility. One such procedure has been recommended for use with discs to test susceptibility to ceftazidime.

Reports from the laboratory giving results of the standard single-disc susceptibility test with a 30 mcg ceftazidime disc should be interpreted according to the following criteria:

- Susceptible organisms produce zones of 18 mm or greater, indicating that the test organism is likely to respond to therapy.

- Organisms that produce zones of 15 mm to 17 mm are expected to be susceptible if high dosage is used or if the infection is confined to tissues and fluids (e.g. urine) in which high antibiotic levels are attained.

- Resistant organisms produce zones of 14 mm or less, indicating that other therapy should be selected.

Organisms should be tested with the ceftazidime disc, since ceftazidime has been shown by in vitro tests to be active against certain strains found resistant when other beta-lactam discs are used.

Standardised procedures require the use of laboratory control organisms. The 30 mcg ceftazidime disc should give zone diameters between 25 mm and 32 mm for E. coli ATCC 25922. For P. aeruginosa ATCC 27853, the zone diameters should be between 22 mm and 29 mm. For S. aureus ATCC 25923, the zone diameters should be between 16 mm and 20 mm.

In other susceptibility testing procedures, e.g. ICS agar dilution or the equivalent, a bacterial isolate may be considered susceptible if the MIC value for ceftazidime is not more than 16 mcg/mL. Organisms are considered resistant to ceftazidime if the MIC is equal to or greater than 64 mcg/mL. Organisms having an MIC value of less than 64 mcg/mL but greater than 16 mcg/mL are expected to be susceptible if high dosage is used or if the infection is confined to tissues and fluids (e.g. urine) in which high antibiotic levels are attained.

As with the standard diffusion methods, dilution procedures require the use of laboratory control organisms. Standard ceftazidime powder should give MIC values in the range of 4 mcg/mL and 16 mcg/mL for S. aureus ATCC 25923. For E. coli ATCC 25922, the MIC range should be between 0.125 mcg/mL and 0.5 mcg/mL.

For P. aeruginosa ATCC 27853, the MIC range should be between 0.5 mcg/mL and 2 mcg/mL.

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

Clinical Trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

The pharmacokinetics of ceftazidime are similar whether it is administered by a single or by repeat dosage.

Concurrent oral administration of probenecid did not affect the serum levels or urinary recoveries of ceftazidime. The pharmacokinetics of ceftazidime were not affected when administered intramuscularly with 0.5% lidocaine (lignocaine).

Absorption

Absorption of ceftazidime after oral administration is negligible; therefore, CEFTAZIDIME VIATRIS is intended for parenteral use only.

In man after a single intramuscular administration of 500 mg and 1 g, mean peak serum levels of 18 and 37 mg/L respectively are achieved at 1 hour falling to 8 and 2 mg/L and 20 and 5 mg/L at 4 and 8 hours respectively for the two doses. Five minutes after an intravenous bolus injection of 500 mg, 1 g and 2 g, mean serum levels are respectively 46, 87 and 170 mg/L falling to 17 and 6 mg/L, 32 and 10 mg/L and 85 and 15 mg/L at 1 and 4 hours respectively with the three doses. The serum half-life in adults with normal renal function is about 1.8 hours (1.2-2.9 hours). This may be prolonged to 20-35 hours in anuric patients. In neonates, the serum half-life of ceftazidime can be 3-4 times greater than that measured in adults. The serum protein binding of ceftazidime is low at about 10%.

Table 3. Mean peak serum concentrations of Ceftazidime following IM administration

	Serum concentrations (mg/L)		
Ceftazidime IM dose	1 hour	4 hours	8 hours
500 mg	18	8	2
1 g	37	20	5

Table 4. Mean peak serum concentrations of Ceftazidime following IV administration

	Serum concentrations (mg/L)		
Ceftazidime IV dose	5 minutes	1 hour	4 hours
500 mg	46	17	6
1 g	87	32	10
2 g	170	85	15

Distribution

The mean maximum concentrations of ceftazidime in bone, heart, bile, sputum, aqueous humour, synovial and pleural and peritoneal fluids were in excess of the *in vitro* minimum inhibitory levels for susceptible organisms (see Section 5.1 PHARMACODYNAMIC PROPERTIES – Mechanism of Action - Susceptibility Tests). Transplacental transfer of the antibiotic readily occurs. Ceftazidime penetrates the intact blood brain barrier poorly and low levels are achieved in the CSF.

Metabolism

Ceftazidime is not metabolised in the body.

Excretion

Ceftazidime is excreted unchanged in the active form into the urine by glomerular filtration. In the presence of normal renal function approximately 80 to 90% of the dose is recovered in the urine within 24 hours. Less than 1% is excreted via the bile.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Sodium carbonate (116.4 mg per gram of ceftazidime).

CEFTAZIDIME VIATRIS contains approximately 54 mg (2.3 mEq) of sodium per gram of ceftazidime.

6.2 INCOMPATIBILITIES

Sodium Bicarbonate Injection 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.

See Section 4.2 DOSE AND METHOD OF ADMINISTRATION - Instructions for reconstitution.

6.3 SHELF LIFE

Vials of unreconstituted CEFTAZIDIME VIATRIS have a shelf-life of 2 years, if stored under the conditions outlined in Section 6.4 SPECIAL PRECAUTIONS FOR STORAGE**.**

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Vials of unreconstituted CEFTAZIDIME VIATRIS should be stored in the original package at a temperature below 25°C. Protect from light.

For storage conditions of the reconstituted solution, see Section 4.2 DOSE AND METHOD OF ADMINISTRATION - Administration.

6.5 NATURE AND CONTENTS OF CONTAINER

CEFTAZIDIME VIATRIS is available in individually cartoned vials.

CEFTAZIDIME VIATRIS containing 1 g ceftazidime (as pentahydrate) is supplied in a type III clear glass vial sealed with a bromobutyl rubber stopper and capped with an aluminium flip-off capsule.

Pack sizes: 1, 5 and 10 vials.

CEFTAZIDIME VIATRIS containing 2 g ceftazidime (as pentahydrate) is supplied in a type III clear glass vial sealed with a bromobutyl rubber stopper and capped with an aluminium flip-off capsule.

Pack sizes: 1 and 10 vials.

Some strengths, pack sizes and/or pack types may not be marketed.

Australian Register of Therapeutic Goods (ARTG)

AUST R 154398 – CEFTAZIDIME VIATRIS ceftazidime 1g (as pentahydrate) powder for injection vial

AUST R 154399 – CEFTAZIDIME VIATRIS ceftazidime 2g (as pentahydrate) powder for injection vial

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

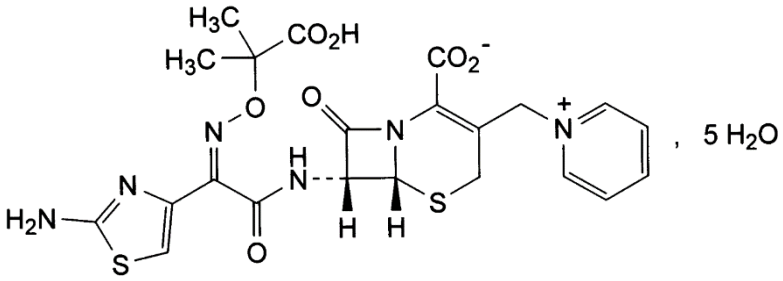
6.7 PHYSICOCHEMICAL PROPERTIES

Ceftazidime pentahydrate is slightly soluble in water and in methanol, practically insoluble in acetone and in alcohol. It dissolves in acid and alkali solutions.

Chemical Structure

Chemical name : (6*R*,7*R*)-7-[[(*Z*)-2-(2-aminothiazol-4-yl)-2-[(1-carboxy-1-methylethoxy)imino] acetyl] amino]8-oxo-3-[(1-pyridinio)methyl]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate pentahydrate.

Structural formula :



Molecular formula : $C_{22}H_{22}N_6O_7S_2,5H_2O$

Molecular weight : 637

CAS Number

78439-06-2

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 - Prescription Only Medicine

8 SPONSOR

Alphapharm Pty Ltd trading as Viatris

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30 – 34 Hickson Road

Millers Point NSW 2000

www.viatris.com.au

Phone: 1800 274 276

9 DATE OF FIRST APPROVAL

21/05/2010

10 DATE OF REVISION

17/01/2024

Summary Table of Changes

Section Changed	Summary of New Information
4.4	Warning for Neurotoxicity added

CEFTAZIDIME VIATRIS_pi\Jan24/00