AUSTRALIAN PRODUCT INFORMATION- CEFTAZIDIME KABI (CEFTAZIDIME AS PENTAHYDRATE)

1 NAME OF MEDICINE
Ceftazidime (as pentahydrate)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
CEFTAZIDIME KABI powder for injection contains either 1 g or 2 g of ceftazidime (as pentahydrate).

Ceftazidime Kabi contains approximately 52.5 mg (2.3 mEq) of sodium per gram of ceftazidime. 1.164g ceftazidime pentahydrate is equivalent to 1 g ceftazidime free acid.

For the full list of excipients, see **Section 6.1 List of excipients.**

3 PHARMACEUTICAL FORM
Powder for injection.

Supplied as a white to pale yellow powder. On the addition of Water for Injections, Ceftazidime Kabi dissolves with effervescence to produce a solution for injection.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Ceftazidime Kabi 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, patients in intensive care units with specific problems, e.g. infected burns.
- **Respiratory tract infections**: for example, pneumonia, broncho-pneumonia, infected pleurisy, infected bronchiectasis, 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), 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 Kabi are supplied under reduced pressure; a positive pressure is produced on reconstitution due to the release of carbon dioxide.

Dosage

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 1–6 g per day: for instance, 500 mg, 1 g or 2 g given twelve or eight hours by intravenous or intramuscular injection.

In urinary tract infections and in many less serious infections, 500 mg or 1 g every twelve hours is usually adequate.

In the majority of infections, 1 g every eight hours or 2 g every twelve hours should be given.

In very severe infections, 2 g every eight or twelve hours should be administered.

Individual doses in excess of 1 g should be administered intravenously.

Children (over 12 months)

The usual dosage range for children aged over 12 months is 25–100 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.

Method of 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 Kabi may be constituted with Water for Injections or, for intramuscular injection, with 1.0% Lidocaine Injection. See table below for addition volumes and solution concentrations.

Preparation of Solution

Vial Size		**Amount of Diluent to be added**	**Approx. Concentration (mg/mL)**
1 g	Intramuscular	3 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. Small bubbles in the reconstituted solution will resolve and a clear solution obtained in about 1–2 minutes. 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 will be 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 (*i.e.* 15–30 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 will be 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 Kabi reconstituted in Water for Injections or 1% Lidocaine Injection retain satisfactory potency for 4 hours if kept below 25°C or for 12 hours if refrigerated (2–8°C).

Ceftazidime is compatible with the intravenous fluids shown below. Solutions at concentrations up to 40 mg/mL in these infusion fluids may be stored for up to 4 hours below 25°C or 12 hours if refrigerated (2-8°C):

- 0.9% Sodium Chloride Infusion
- Compound Sodium Lactate Infusion
- 10% Glucose Infusion

Sodium Bicarbonate Infusion is not recommended as a diluent.

It is advisable to administer reconstituted product as soon as possible.

The dilution is to be made under aseptic conditions. The solution is to be inspected visually for particulate matter prior to administration. The solution should only be used if it is clear and free from particles.

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.

For use in one patient on one occasion only. Discard any unused solution appropriately.

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.

Dosage in Impaired Renal Function

Adults

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 i.e. glomerular filtration rate (GFR) greater than 50 mL/min. In patients with suspected renal insufficiency, an initial loading dose of 1 g ceftazidime may be given. An estimate of GFR should be made to determine the appropriate maintenance dose.

Recommended maintenance doses are shown below.

Recommended Maintenance Doses of Ceftazidime in Renal Insufficiency

Creatinine Clearance (mL/min)	Approx. Serum Creatinine[#] (micromol/L)	Recommended Unit Dose of Ceftazidime (g)	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 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: Creatinine clearance (mL/min) = $\frac{\text{Weight (kg)} \times (140 - \text{age in years}) \times 88.4}{72 \times \text{serum creatinine (micromol/L)}}$

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 removed approximately 10% of the antibiotic when the dwell time was 4–6 hours.

Children

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 three 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 four to six hours.

Dosage adjustment in the elderly

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

4.3 Contraindications

Hypersensitivity to cephalosporins or major allergy to penicillin (anaphylaxis, angioneurotic oedema, urticaria).

Lignocaine should not be used as a diluent for intramuscular injection in patients who are hypersensitive to lignocaine.

4.4 Special warnings and precautions for use

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, 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.

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.

Resistance to initially susceptible *Ente*robacter species and Serratia species can develop during treatment with ceftazidime. When clinically appropriate during therapy of such infections, periodic susceptibility testing should be considered.

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.

Vials of Ceftazidime Kabi injection, 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.

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.

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

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 **4.2 DOSE AND METHOD OF ADMINISTRATION).**

Elevated levels of ceftazidime in patients with renal insufficiency can lead to seizures, encephalopathy, asterixis, neuromuscular excitability and myoclonia. Continued dosage should be determined by degree of renal impairment, severity of infection and susceptibility of the causative organism.

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.

For laboratory tests associated with ceftazidime administration, ceftazidime pentahydrate should be used.

4.5 Interactions with other medicines and other forms of interactions

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.

Nephrotoxicity has been reported following concomitant administration of cephalosporins with aminoglycoside antibiotics or potent diuretics such as frusemide. Renal function should be carefully monitored, especially if higher dosages of the aminoglycosides are to be administered or if therapy is prolonged, because of the potential nephrotoxicity and ototoxicity of aminoglycoside antibiotics. Nephrotoxicity and ototoxicity were not noted when ceftazidime was given alone in clinical trials.

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

4.6 Fertility, pregnancy and lactation

Effects on fertility

No Data available

Use in pregnancy

Pregnancy 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 **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.
Not known: DRESS syndrome[#]

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.

Other (frequency not known)

Hypersensitivity

Maculopapular or urticarial rash, fever, pruritus; very rarely angioedema and anaphylaxis (including bronchospasm and hypotension), erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis.

Hot flushes, superficial desquamation around injection site.

[#] DRESS syndrome (Drug Reaction/Rash with Eosinophilia and Systemic Symptoms). There have been rare reports where DRESS has been associated with ceftazidime.

Reporting of 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 http://www.tga.gov.au/reporting-problems.

4.9 Overdose

Symptoms

Overdosage can lead to neurological sequelae including encephalopathy, convulsions and coma.

Treatment

Ceftazidime can be removed by haemodialysis.

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia) or 0800 764 766 (New Zealand).

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 cephalothin-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 influenza (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 µg 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 15–17 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 µg ceftazidime disc should give zone diameters between 25–32 mm for *E. coli* ATCC 25922. For *P. aeruginosa* ATCC 27853, the zone diameters should be between 22–29 mm. For *S. aureus* ATCC 25923, the zone diameters should be between 16–20 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 ≤ 16 µg/mL. Organisms are considered resistant to ceftazidime if the MIC is ≥ 64 µg/mL. Organisms having an MIC value of < 64 µg/mL but > 16 µg/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 4–16 µg/mL for *S. aureus* ATCC 25923. For *E. coli* ATCC 25922, the MIC range should be between 0.125–0.5 µg/mL. For *P. aeruginosa* ATCC 27853, the MIC range should be between 0.5–2 µg/mL.

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

Clinical trials
No data available.

5.2 Pharmacokinetic properties

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

Distribution
In humans after a single intramuscular administration of 0.5 g 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 & 20 and 5 mg/L at 4 and 8 hours, respectively, for the two doses. Five minutes after an intravenous bolus injection of 0.5 g, 1 g and 2 g, mean serum levels are 46, 87 and 170 mg/L respectively, for the three doses, falling to 17, 32 and 85 mg/L at 1 hour & 6, 10 and 15 mg/L at 4 hours respectively, for the three doses.

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 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.

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

Metabolism
Ceftazidime is not metabolised in the body and is excreted unchanged in the active form into the urine by glomerular filtration.

Excretion
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%.

In the presence of normal renal function approximately 80–90% of the dose is recovered in the urine within 24 hours. Less than 1% is excreted via the bile.

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% lignocaine.

5.3 Preclinical safety data
Genotoxicity
A mouse Micronucleus test and Ames test were both negative for mutagenic effects.

Carcinogenicity
Long-term studies in animals have not been performed to evaluate carcinogenic potential.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Sodium carbonate.

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.

For information on interactions with other medicines and other forms of interactions, refer to Section 4.5.

6.3 Shelf life
In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 Special precautions for storage
Store below 25°C. Protect from light.

6.5 Nature and contents of container
Each vial of unreconstituted Ceftazidime Kabi contains a white or pale yellow powder containing 1 g or 2 g ceftazidime (as pentahydrate).
Vials (Type II colourless glass, halobutyl rubber stopper, plastic-aluminium cap): packs of 1, 5 and 10.

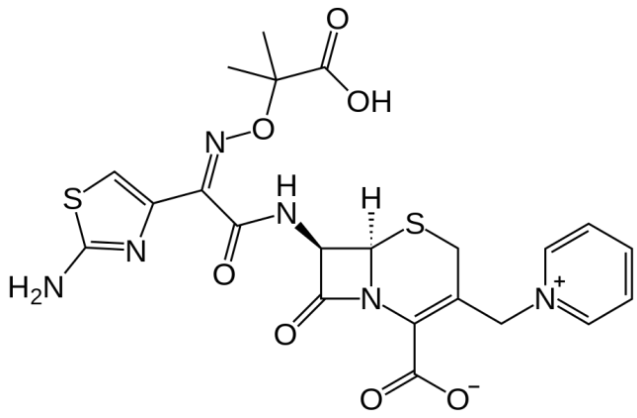
Not all strengths and/or pack sizes may be marketed in Australia.

6.6 Special precautions for disposal

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 Physicochemical properties

Chemical structure



·5H_2O

Chemical Name: (6*R*,7*R*)-7-[[(2*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.

Molecular Formula: $C_{22}H_{22}N_6O_7S_2 \cdot 5H_2O$

Molecular Weight: 636.65

CAS number
78439-06-2

7 MEDICINE SCHEDULE (POISONS STANDARD)

Australia: S4 – Prescription Only Medicine

8 SPONSOR

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9 DATE OF FIRST APPROVAL

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10 DATE OF REVISION OF THE TEXT

29 January 2024

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	Deleted header from page 2-14
4.1, 4.2	Minor editorial changes
4.4	Addition of neurotoxicity section
8	Removal of NZ details