PRODUCT INFORMATION

CEFTAZIDIME KABI Powder for Injection

NAME OF THE MEDICINE

Ceftazidime (as pentahydrate)


Chemical Structure:

![Chemical Structure Image]

Molecular Formula: C_{22}H_{22}N_{6}O_{7}S_{2}

Molecular Weight: 636.65

CAS Registry Number: 78439-06-2

DESCRIPTION

Ceftazidime is a cephalosporin antibiotic for use by injection only. It is supplied as a white or pale yellow powder in vials containing 1 g and 2 g ceftazidime (as pentahydrate) with sodium carbonate (121.2 mg per gram ceftazidime). On the addition of Water for Injections, Ceftazidime Kabi dissolves with effervescence to produce a solution for injection.

Ceftazidime Kabi contains approximately 52.5 mg (2.3 mEq) of sodium per gram of ceftazidime. 1.164 g ceftazidime pentahydrate is equivalent to 1 g ceftazidime free acid. For laboratory tests associated with ceftazidime administration, ceftazidime pentahydrate should be used.

PHARMACOLOGY

Pharmacokinetics

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

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

The mean maximum concentrations of ceftazidime in bone, heart, bile, sputum, aqueous humour, synovial and pleural and peritoneal fluids were in excess of the \textit{in vitro} minimum inhibitory levels for susceptible organisms (see \textbf{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.

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.

**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 \textit{in vitro} activity against the following organisms:

- **Gram-negative**
  - \textit{Pseudomonas aeruginosa}
  - \textit{Pseudomonas} species (other)
  - \textit{Klebsiella pneumoniae}
  - \textit{Klebsiella} species (other)
  - \textit{Proteus mirabilis}
  - \textit{Proteus vulgaris}
  - \textit{Morganella morganii} (formerly \textit{Proteus morganii})
  - \textit{Proteus retgeri}
  - \textit{Providencia} species
  - \textit{Escherichia coli}
  - \textit{Enterobacter} species
  - \textit{Citrobacter} species
  - \textit{Serratia} species
  - \textit{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 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.

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

INDICATIONS

Ceftazidime 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), bacteremia, 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.

CONTRAINDICATIONS

Ceftazidime is contraindicated in persons who have shown hypersensitivity to cephalosporins or who have experienced a 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.
PRECAUTIONS

Warnings
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.

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. 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.

**Resistance to initially susceptible Enterobacter species and Serratia species can develop during treatment with ceftazidime.**
Patients with Impaired Renal Function

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 DOSAGE AND ADMINISTRATION).

Use in Patients with Impaired Liver Function

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.

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 Kabi are supplied under reduced pressure; a positive pressure is produced on reconstitution due to the release of carbon dioxide. See DOSAGE AND ADMINISTRATION for recommended techniques of reconstitution.

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

Use in Pregnancy


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

Effect 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, Clinithest) may be observed. Ceftazidime does not interfere in the alkaline picrate assay for creatinine.

INTERACTIONS WITH OTHER MEDICINES
Concurrent use of high doses with nephrotoxic drugs may adversely affect renal function (see PRECAUTIONS, Warnings).

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.

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

ADVERSE 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 \( \geq 1/10 \)
- common \( \geq 1/100 \) to \(< 1/10 \)
- uncommon \( \geq 1/1,000 \) to \(< 1/100 \)
- rare \( \geq 1/10,000 \) 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 PRECAUTIONS, Warnings).

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.
DOSAGE AND 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.

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 1–6 g per day: for instance, 0.5 g, 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, 0.5 g 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 in excess of 1 g should be administered intravenously.

Infants and Children
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.

Ceftazidime Administered in Children via I.V. bolus, 12-hourly:
Volume (mL) of each divided dose

<table>
<thead>
<tr>
<th>Vial Size</th>
<th>1 g (made up with 10 mL diluent)</th>
<th>2 g (made up with 10 mL diluent)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Concentration: 90 mg/mL</td>
<td>Concentration: 170 mg/mL</td>
</tr>
<tr>
<td>Dose</td>
<td>25</td>
<td>50</td>
</tr>
<tr>
<td>Body Weight (kg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>0.45 mL</td>
<td>0.85 mL</td>
</tr>
<tr>
<td>4</td>
<td>0.60 mL</td>
<td>1.15 mL</td>
</tr>
<tr>
<td>5</td>
<td>0.70 mL</td>
<td>1.40 mL</td>
</tr>
<tr>
<td>6</td>
<td>0.85 mL</td>
<td>1.70 mL</td>
</tr>
<tr>
<td>10</td>
<td>1.40 mL</td>
<td>2.80 mL</td>
</tr>
<tr>
<td>20</td>
<td>2.80 mL</td>
<td>5.60 mL</td>
</tr>
<tr>
<td>30</td>
<td>4.20 mL</td>
<td>8.35 mL</td>
</tr>
<tr>
<td>40</td>
<td>5.60 mL</td>
<td>11.15 mL</td>
</tr>
<tr>
<td>50</td>
<td>6.95 mL</td>
<td>13.90 mL</td>
</tr>
<tr>
<td>60</td>
<td>8.35 mL</td>
<td>16.70 mL</td>
</tr>
</tbody>
</table>

Shaded volumes represent where more than one vial of the nominated strength needs to be used.
Ceftazidime Administered in Children via I.V. bolus, 8-hourly:
Volume (mL) of each divided dose

<table>
<thead>
<tr>
<th>Vial Size</th>
<th>1 g (made up with 10 mL diluent)</th>
<th>2 g (made up with 10 mL diluent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentration</td>
<td>90 mg/mL</td>
<td>170 mg/mL</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dose (mg/kg/day)</th>
<th>25</th>
<th>50</th>
<th>100</th>
<th>25</th>
<th>50</th>
<th>100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Weight (kg)</td>
<td>3</td>
<td>0.30 mL</td>
<td>0.60 mL</td>
<td>1.15 mL</td>
<td>0.15 mL</td>
<td>0.30 mL</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.40 mL</td>
<td>0.75 mL</td>
<td>1.50 mL</td>
<td>0.20 mL</td>
<td>0.40 mL</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>0.50 mL</td>
<td>0.95 mL</td>
<td>1.90 mL</td>
<td>0.25 mL</td>
<td>0.50 mL</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>0.60 mL</td>
<td>1.15 mL</td>
<td>2.25 mL</td>
<td>0.30 mL</td>
<td>0.60 mL</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>0.95 mL</td>
<td>1.90 mL</td>
<td>3.75 mL</td>
<td>0.50 mL</td>
<td>1.00 mL</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>1.90 mL</td>
<td>3.75 mL</td>
<td>7.45 mL</td>
<td>1.00 mL</td>
<td>2.00 mL</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>2.80 mL</td>
<td>5.60 mL</td>
<td>11.15 mL</td>
<td>1.50 mL</td>
<td>2.95 mL</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>3.75 mL</td>
<td>7.45 mL</td>
<td>14.85 mL</td>
<td>2.00 mL</td>
<td>3.95 mL</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>4.65 mL</td>
<td>9.30 mL</td>
<td>18.55 mL</td>
<td>2.50 mL</td>
<td>4.95 mL</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>5.60 mL</td>
<td>11.15 mL</td>
<td>22.25 mL</td>
<td>2.95 mL</td>
<td>5.90 mL</td>
</tr>
</tbody>
</table>

shaded volumes represent where more than one vial of the nominated strength needs to be used.

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 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

<table>
<thead>
<tr>
<th>Creatinine Clearance (mL/min)</th>
<th>Approx. Serum Creatinine# (micromol/L)</th>
<th>Recommended Unit Dose of Ceftazidime (g)</th>
<th>Frequency of Dosing (hourly)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50–31</td>
<td>150–200</td>
<td>1.0</td>
<td>12</td>
</tr>
<tr>
<td>30–16</td>
<td>200–350</td>
<td>1.0</td>
<td>24</td>
</tr>
<tr>
<td>15–6</td>
<td>350–500</td>
<td>0.5</td>
<td>24</td>
</tr>
<tr>
<td>≤ 5</td>
<td>500</td>
<td>0.5</td>
<td>48</td>
</tr>
</tbody>
</table>

# 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 \times \text{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.

**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

<table>
<thead>
<tr>
<th>Vial Size</th>
<th>Amount of Diluent to be added</th>
<th>Approx. Concentration (mg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 g</td>
<td>Intramuscular 3 mL</td>
<td>260</td>
</tr>
<tr>
<td></td>
<td>Intravenous 10 mL</td>
<td>90</td>
</tr>
<tr>
<td>2 g</td>
<td>Intravenous bolus 10 mL</td>
<td>170</td>
</tr>
<tr>
<td></td>
<td>Intravenous infusion 50 mL#</td>
<td>40</td>
</tr>
</tbody>
</table>

# 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.

OVERDOSAGE
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 Poison Information Centre on 13 11 26 (Australia).

PRESENTATION AND STORAGE CONDITIONS
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.

Storage
Store below 25°C. Protect from light.

NAME AND ADDRESS OF THE SPONSOR
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POISON SCHEDULE OF THE MEDICINE
S4 – Prescription Only Medicine
DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS
2 Jul 2015

DATE OF MOST RECENT AMENDMENT
28 Apr 2016