**HOSPIRA™ CEFTAZIDIME, POWDER FOR INJECTION**

**NAME OF THE MEDICINE**
Ceftazidime (as ceftazidime pentahydrate)

![Chemical Structure](image)

CAS No. 78439-06-2

Molecular Weight: 636.6

Molecular formula: C_{22}H_{22}N_{6}O_{7}S_{2}, 5H_{2}O

Chemical name:

**DESCRIPTION**
Hospira™ Ceftazidime Powder for Injection is a cephalosporin antibiotic for use by injection only. It is supplied as a white to cream coloured crystalline powder in vials containing 1 g and 2 g ceftazidime (as pentahydrate) with sodium carbonate anhydrous (117 mg per gram of ceftazidime). On the addition of Water for Injections, Hospira™ Ceftazidime Powder for Injection dissolves with effervescence to produce a light yellow to amber coloured solution for injection.

Ceftazidime pentahydrate is slightly soluble in water and in methanol, practically insoluble in acetone and in ethanol (96 per cent). It dissolves in acid and alkali solutions. Ceftazidime pentahydrate decomposes at about 150 °C.

Ceftazidime pentahydrate is hygroscopic and crystalline in nature. No potential polymorphism is reported.

Hospira™ Ceftazidime Powder for Injection contains approximately 51 mg (2.17 mEq) of sodium per gram of ceftazidime. 116 mg ceftazidime pentahydrate is equivalent to 100 mg ceftazidime anhydrous. For laboratory tests associated with ceftazidime administration, ceftazidime pentahydrate should be used.

**PHARMACOLOGY**

**Pharmacokinetics**
Absorption of ceftazidime after oral administration is negligible, therefore Hospira™ Ceftazidime Powder for Injection is intended for parenteral use only.
In humans, 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 four and eight hours respectively for the two doses.

See the table below.

**Mean serum concentrations of ceftazidime following IM administrations**

<table>
<thead>
<tr>
<th>Ceftazidime IM dose</th>
<th>1 hour</th>
<th>4 hour</th>
<th>8 hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 mg</td>
<td>18</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>1 g</td>
<td>37</td>
<td>20</td>
<td>5</td>
</tr>
</tbody>
</table>

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 one and four hours respectively with the three doses. See the table below.

**Mean serum concentrations of ceftazidime after an IV bolus injection**

<table>
<thead>
<tr>
<th>Ceftazidime IM dose</th>
<th>5 minute</th>
<th>1 hour</th>
<th>4 hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 mg</td>
<td>46</td>
<td>17</td>
<td>6</td>
</tr>
<tr>
<td>1 g</td>
<td>87</td>
<td>32</td>
<td>10</td>
</tr>
<tr>
<td>2 g</td>
<td>170</td>
<td>85</td>
<td>15</td>
</tr>
</tbody>
</table>

The serum half life in adults with normal renal function is about 1.8 hours (1.2 to 2.9 hours). This may be prolonged to 20 to 35 hours in anuric patients. In neonates, the serum half life of ceftazidime can be 3 to 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 to 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 *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.

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 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: Disc Susceptibility Test**

**Dilution or diffusion techniques** – either quantitative (minimum inhibitory concentration (MIC)) or breakpoint should be used following a regularly updated, recognised and standardised method (e.g. NCCLS). Standardised susceptibility test procedures require the use of laboratory control microorganisms to control the technical aspects of the laboratory procedures.

A report of “Susceptible” indicates that the pathogen is likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable. A report of “Intermediate” indicates that the result should be considered equivocal, and if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer zone, which prevents small-uncontrolled technical factors
from causing major discrepancies in interpretation. A report of “Resistant” indicates that the pathogen is not likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable; other therapy should be selected.

Note: The prevalence of resistance may vary geographically for selected species and local information on resistance is desirable, particularly when treating severe infections.

**INDICATIONS**

Hospira™ Ceftazidime Powder for Injection 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, for example 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.
- Infections associated with haemo- and peritoneal dialysis and with continuous ambulatory peritoneal dialysis (CAPD).

**CONTRAINDICATIONS**

Hospira™ Ceftazidime Powder for Injection is contraindicated in persons who have shown hypersensitivity to cephalosporins or who have experienced a major allergy to penicillin (anaphylaxis, angioneurotic oedema, urticaria).

Ceftazidime should not be administered to patients with a known hypersensitivity to the excipient Sodium carbonate anhydrous.

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

**PRECAUTIONS**

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. 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.

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 can develop during treatment with ceftazidime.

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.

Prescribing ceftazidime in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Inducible type I beta-lactamase resistance has been noted with some organisms (e.g. *Enterobacter* spp., *Pseudomonas* spp., and *Serratia* spp.). As with other extended-spectrum beta-lactam antibiotics, resistance can develop during therapy, leading to clinical failure in some cases. When treating infections caused by these organisms, periodic susceptibility testing should be performed when clinically appropriate. If patients fail to respond to monotherapy, an aminoglycoside or similar agent should be considered.

Cephalosporins may be associated with a fall in prothrombin activity. Those at risk include patients with renal and hepatic impairment, or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy. Prothrombin time should be monitored in patients at risk and exogenous vitamin K administered as indicated.

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

**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**). 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 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 IM 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.

Carcinogenesis, Mutagenesis, Impairment of Fertility.
Long term studies in animals have not been performed to evaluate carcinogenic potential. However, a mouse Micronucleus test and Ames test were both negative for mutagenic effects.

**Use in 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.

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

**Effects on ability to drive and use machines**
During treatment with Ceftazidime, undesirable effects may occur (e.g. dizziness) which may influence the ability to drive and use machines. Patients should be cautious when driving or operating machinery.

**Interactions with Other Medicines**

*Chloramphenicol*
Chloramphenicol is antagonistic in vitro to 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 literature that concurrent use of two beta-lactam antibiotics may exhibit antagonism.

*Aminoglycoside antibiotics and/or diuretics*
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 aminoglycosidic antibiotics. Nephrotoxicity and ototoxicity were not noted when ceftazidime was given alone in clinical trials.

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†Category B1: Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformations or other direct or indirect harmful effects on the human foetus having been observed. Studies in animals have not shown evidence of an increased occurrence of foetal damage.
In common with other antibiotics, ceftazidime may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.

**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, Fehling’s, Clinitest) may be observed.

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

**ADVERSE EFFECTS**
Clinical trial experience has shown that ceftazidime is generally well tolerated.

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 and <1/10,
- uncommon ≥1/1000 and <1/100,
- rare ≥1/10,000 and <1/1000,
- 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). Angioedema.

**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 IV administration.

Cutaneous vasculitis has also been reported

**Gastrointestinal disorder**

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 Warnings and Precautions)...

**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 IM 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.

**Miscellaneous**

Hot flushes, superficial desquamation around injection site.

**DOSAGE AND ADMINISTRATION**

Note: Vials of Hospira™ Ceftazidime Powder for Injection 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 IV or IM 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, particularly in immunocompromised patients including those with neutropenia, 2 g every 8 or 12 hours, or 3 g every 12 hours should be administered.

In fibrocystic adults with pseudomonal lung infections, 100 to 150 mg/kg/day in 3 divided doses should be administered.

In adults with normal renal function 9 g/day has been used without ill effect. Individual doses in excess of 1 g should be administered intravenously.

**Infants and children (> 2 months):**
30 to 100 mg/kg/day in 2 or 3 divided doses.

Doses of up to 150 mg/kg/day (maximum 6 g/day) in 3 divided doses may be given to children with very serious infections e.g. those who are immunocompromised or who suffer from cystic fibrosis.

**Neonates (0 - 2 months):**
25-60 mg/kg/day in 2 divided doses.

In neonates the serum half life of ceftazidime can be 3 to 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.

**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 of ceftazidime may be given. An estimate of GFR should be made to determine the appropriate maintenance dose. See table 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 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:**

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

**Females:** Multiply above value by 0.85.

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 to 5 hours. The appropriate maintenance dose of ceftazidime should be repeated following each haemodialysis period.

**Peritoneal dialysis**

Ceftazidime may be used in peritoneal dialysis and continuous ambulatory peritoneal dialysis (CAPD).

In addition to intravenous use, ceftazidime can be incorporated into the dialysis fluid (usually 125 to 250 mg for 2 litres of dialysis solution).

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

For patients on venovenous haemofiltration and venovenous haemodialysis, follow the dosage recommendations in the following tables:
Continuous venovenous haemofiltration dosage guidelines for ceftazidime

<table>
<thead>
<tr>
<th>Residual renal function (creatinine clearance in mL/min)</th>
<th>Maintenance dose (mg) for an ultrafiltration rate (mL/min) of $^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>16.7</td>
</tr>
<tr>
<td>5</td>
<td>250</td>
</tr>
<tr>
<td>10</td>
<td>250</td>
</tr>
<tr>
<td>15</td>
<td>250</td>
</tr>
<tr>
<td>20</td>
<td>500</td>
</tr>
</tbody>
</table>

$^a$ Maintenance dose to be administered every 12 hours.

Ceftazidime dosage guidelines during continuous venovenous haemodialysis

<table>
<thead>
<tr>
<th>Residual renal function (creatinine clearance in mL/min)</th>
<th>Maintenance dose (mg) for a dialysate inflow rate of $^a$:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0 litres/h</td>
<td>2.0 litres/h</td>
</tr>
<tr>
<td>Ultrafiltration rate (litres/h)</td>
<td>Ultrafiltration rate (litres/h)</td>
</tr>
<tr>
<td>0.5</td>
<td>1.0</td>
</tr>
<tr>
<td>5</td>
<td>500</td>
</tr>
<tr>
<td>10</td>
<td>500</td>
</tr>
<tr>
<td>15</td>
<td>500</td>
</tr>
<tr>
<td>20</td>
<td>750</td>
</tr>
</tbody>
</table>

$^a$ Maintenance dose to be administered every 12 hours.

**Administration**

Hospira™ Ceftazidime Powder for Injection 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:**

Hospira™ Ceftazidime Powder for Injection may be reconstituted with Water for Injections or, for intramuscular injection, with 1.0% or 0.5% 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.
Preparation of Solution

<table>
<thead>
<tr>
<th>Vial size/route</th>
<th>Amount of diluent to be added</th>
<th>Approximate concentration (mg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 g – intramuscular</td>
<td>3.0 mL</td>
<td>260</td>
</tr>
<tr>
<td>1 g – intravenous</td>
<td>10.0 mL</td>
<td>90</td>
</tr>
<tr>
<td>2 g – intravenous bolus</td>
<td>10.0 mL</td>
<td>170</td>
</tr>
<tr>
<td>2 g – intravenous infusion</td>
<td>50.0 mL#</td>
<td>40</td>
</tr>
</tbody>
</table>

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

All sizes of vials are supplied 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 IM/IV and 2 g IV 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 to 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 IV 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 to 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. Additional pressure that may develop in the vial especially after, storage should be relieved prior to administration to the patient.

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 Hospira™ Ceftazidime Powder for Injection reconstituted in Water for Injections retains satisfactory potency for up to 24 hours if kept refrigerated (2 to 8°C).
Ceftazidime is also compatible with the following intravenous fluids:

0.9% Sodium Chloride Injection BP,

5% Glucose Injection BP,

0.9% Sodium Chloride with 5% Glucose Injection BP (1:1, V/V),

M/6 Sodium Lactate Injection BP,

M/6 Compound Sodium Lactate Injection BP (Hartmann’s Solution),

Dextran 40 Injection BP 10% in 0.9% Sodium Chloride Injection,

Dextran 40 Injection BP 10% in 5% Glucose,

Dextran 70 Injection BP 6% in 0.9% Sodium Chloride,

Dextran 70 Injection BP 6% in 5% Glucose Injection BP.

Solutions in these infusion fluids may be stored for up to 24 hours if refrigerated (2 to 8°C).

Hospira™ Ceftazidime Powder for Injection may be reconstituted for intramuscular administration using 0.5% and 1.0% Lignocaine Hydrochloride Injection BP, the resultant solutions may be stored for up to 24 hours under refrigeration (2 to 8°C).

Some increase in the colour of prepared solutions of Hospira™ Ceftazidime Powder for Injection may occur on storage. It is, however, advisable to use the reconstituted product as soon as possible.

Sodium Bicarbonate Injection is not recommended as a diluent.

Ceftazidime 2g injection may be stored for up to 24 hours under refrigeration (2 to 8 °C) at concentrations between 0.05 mg/mL and 0.25 mg/mL in Intraperitoneal Dialysis Fluid (Lactate) BPC 1973.

Ceftazidime 2g injection has been found compatible for 24 hours under refrigeration (2 to 8°C) when admixture at 4 mg/mL with potassium chloride 10 mEq/L or 40 mEq/L in 0.9% Sodium Chloride Injection BP, or heparin (10 and 50 units/mL) in 0.9% sodium chloride.

Ceftazidime 2g injection (4 mg/mL) has been found compatible for 24 hours when refrigerated (2 to 8°C, do not freeze) when admixed with cloxacillin.

Ceftazidime 2 g injection (5 mg/mL) is compatible for 24 hours when refrigerated (2 to 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.
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.

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

In case of overdose, immediately contact the Poisons Information Centre on 13 11 26 (Australia) or 0800 764 766 (New Zealand) for advice on management.

**PRESENTATION AND STORAGE CONDITIONS**
Hospira™ Ceftazidime Powder for Injection containing ceftazidime (as pentahydrate) 1 g/vial is available in 1 vial per pack as a white to off white powder, filled in 20 ml clear glass moulded Type 1 vial, sealed with a grey bromo butyl rubber stopper and flip-off seal.

Hospira™ Ceftazidime Powder for Injection containing ceftazidime (as pentahydrate) 2 g/vial is available in 1 vial per pack as a white to off white powder, filled in 100 ml clear glass moulded Type 1 vial, sealed with a grey bromo butyl rubber stopper and flip-off seal.

Vials of unreconstituted Hospira™ Ceftazidime Powder for Injection should be stored at a temperature below 25°C and protected from light.

**MEDICINE CLASSIFICATION**
Prescription Medicine

**NAME AND ADDRESS OF THE SPONSOR**
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Toll Free Number: 0800 736 363

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