In this leaflet:

Parzidim 1 g - vial:

1 vial with ceftazidime pentahydrate contains 1.1648 g, equivalent to 1 g ceftazidime

Pharmaceutical form: Powder for preparing a solution for injection/infusion.
White to off-white powder

Presentations: Single packs of 1 vial + solvent,
Hospital packs of 10, 25 and 50 vials

- The active substance is ceftazidime
- The other ingredient is anhydrous sodium carbonate.

Marketing authorization holder and manufacturer: Sandoz GmbH, Kundl, Austria

1. WHAT PARZIDIM IS AND WHAT IT IS USED FOR

The agent inhibits the formation of the cell wall in bacteria, which kills the microbes. The active substance has strong antibacterial activity on Gram-negative microbes (e.g. Haemophilus influenzae, Haemophilus parainfluenzae, Escherichia coli, Salmonella sp.), but also on some Gram-positive organisms (e.g. streptococci, staphylococci) and is also resistant to those bacteria which produce a substance (beta-lactamase) that inactivates some antibiotics.

Ceftazidime is suitable for parenteral treatment of the following infections, provided they are caused by ceftazidime-sensitive microbes:

- infections of the respiratory tract, including infections of the lower respiratory tract in patients with cystic fibrosis (a congenital metabolic disorder)
- infections of the urinary tract: ceftazidime may also be administered through the urethra for prophylaxis before surgical removal of the prostate gland
- infections of the skin and soft tissue
- infections of the biliary tract
- infections of the abdominal cavity
- infections of the bones and joints
- infections associated with peritoneal dialysis and continuous ambulatory peritoneal dialysis (CAPD) (procedure for cleansing the blood)
- inflammation of the membranes of the brain (meningitis) caused by aerobic Gram-negative organisms

It is recommended to wait for the results from bacterial cultures and sensitivity testing before treatment is initiated. This is important in particular if ceftazidime is to be used for monotherapy.

For the treatment of infections presumably caused by a mix of sensitive and resistant species, ceftazidime is to be used in combination with one or more other antibacterial drugs. In case of infections presumably caused by aerobic and anaerobic bacteria, for example, combination therapy with one antibacterial agent against anaerobics should be considered. Ceftazidime may also be combined with another antibacterial active substance (such as an aminoglycoside) for treating infections in patients with severe blood count abnormality.

Official and national recommendations on adequate use of antibacterial products must be taken into account.

2. BEFORE YOU USE PARZIDIM

Do not use Parzidim:

- If you are hypersensitive (allergic) to ceftazidime, to cephalosporins or to sodium carbonate.
- If you have a history of immediate allergic reactions and/or severe hypersensitivity reactions to a penicillin or another β-lactam.

Take special care with Parzidim:

Before starting treatment with ceftazidime, it is necessary to carefully establish a history of previous hypersensitivity reactions to ceftazidime, cephalosporins, penicillins or other β-lactam products. Ceftazidime must not be used in patients with a history of hypersensitivity to any cephalosporin. It may likewise not be used in patients developing immediate hypersensitivity reactions and/or severe hypersensitivity reactions to any penicillin or any other β-lactam product. Caution is advised when ceftazidime is used in patients developing any other type of hypersensitivity reaction to a penicillin or any other β-lactam product.

Both antibiotics-related diarrhoea and inflammation of the large intestine (colitis and pseudomembranous colitis) have been observed in conjunction with ceftazidime use. These diagnoses must be considered for all patients suffering from diarrhoea during or shortly after treatment. If severe and/or bloody diarrhoea occurs during treatment, ceftazidime must nevertheless be considered in cases where coadministration of ceftazidime with chloramphenical (or with other bacteriostatic agents, e.g. with tetracycline or sulphonamide) is proposed.

3. HOW TO USE PARZIDIM

Parzidim may be administered only by a doctor.

Parzidim is available in 500 mg and 1 g strengths for different dosages.

For more detailed information see section 6. Notes on handling and use for doctors and healthcare professionals.

If you have the impression that the effect of Ceftazidim is too strong or too weak, talk to your doctor or pharmacist.

If you use more Ceftazidim than you should:

A ceftazidime overdose may cause pain, inflammation and venous inflammation at the injection site.

In patients with kidney failure, an overdose or the administration of excessively large doses may be followed by neurological symptoms such as dizziness, impaired skin sensation, headache, brain damage, convulsions and coma.

Changes in laboratory findings which may be caused by an overdosage include a rise in creatinine, BUN, liver enzymes and bilirubin, a positive Coombs test, thrombocytosis, thrombocytopenia, eosinophilia, leucopenia and prolonged prothrombin time.

General symptomatic and supportive therapeutic measures must be instituted, alongside specific measures to control any convulsions. In the event of a large overdosage, in patients with renal failure in particular, combined treatment with haemodialysis and haemoperfusion must be considered.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Parzidim can have side effects. The most common side effects of ceftazidime treatment are local reactions to intravenous injections, allergic reactions and effects on the gastrointestinal tract.

Infections and infestations
Fungal growth (candidiasis) and acute or chronic inflammation of the vagina.

Blood and lymphatic system disorders
Changes in blood counts (eosinophilia, haemolytic anaemia, thrombocytosis).
There have been very few reports of a reduced number of white blood cells (leukopenia), a markedly reduced number of certain white blood cells (agranulocytosis, neutropenia), a reduced number of platelets (thrombocytopenia) and lymphocytosis.

Immune system disorders
Itching, skin rash, nettle rash, skin rashes of various intensity (erythema multiforme) and fever. Severe skin disorders (toxic epidermal necrolysis and Stevens-Johnson syndrome) were observed in a few cases. Swelling of the skin and mucous membranes (angioneurotic oedema) and hypersensitivity symptoms (asthma-like breathing difficulty and/or low blood pressure) have been observed in very few cases.

Nervous system disorders
Headache, dizziness, impaired skin sensation and taste disturbance. Patients with impaired kidney function were reported to develop neurological symptoms such as tremor, muscle jerks, convulsions, brain damage and coma after receiving a ceftazidime dose which had not been appropriately reduced.

Gastrointestinal disorders
Diarrhoea, nausea, vomiting and abdominal pain. Oral thrush and inflammation of the large intestine (pseudomembranous colitis).

Liver and biliary system disorders
Rise in one or more liver enzyme values: AST (SGOT), ALT (SGPT), LDH, GGT and alkaline phosphatase. Very rarely jaundice.

Skin and subcutaneous cellular tissue disorders
See Immune system disorders

Kidney and urinary system disorders
A transient rise in blood urea, BUN and/or serum creatinine were observed occasionally.

Generalized disorders and administration site reactions
Fever.
Venous inflammation or acute formation of a blood clot in the superficial veins with inflammatory reaction of the vessel wall (thrombophlebitis), pain and/or inflammation at the injection site.

Investigations
Positive Coombs test
If you notice any side effects not mentioned in this

The duration of treatment depends on the patient's response. Treatment should generally be continued for at least 48 hours after clinical recovery.

Dosage in the presence of kidney failure: Ceftazidime is eliminated almost exclusively via glomerular filtration; the dose must be reduced if the glomerular filtration rate (GFR) is below 50 ml/min.
For adults with impaired kidney function, the initial ceftazidime dose may be 1 g, followed by an adequate maintenance dose, see table:

Recommended ceftazidime maintenance dose for adults with impaired kidney function

Creatinine clearance ml/min	Serum creatinine (approximate)* µmol/l (mg/dl)	Recommended single dose of ceftazidime (g)	Dosing interval (hours)
50-31	150-200 (1.7-2.3)	1	12
30-16	200-350 (2.3-4.0)	1	24
15-6	350-500 (4.0-5.6)	0.5	24
<5	>500 (>5.6)	0.5	48

* These values are guidelines and may not accurately reflect the kidney function in all patients, especially in elderly patients in whom the serum creatinine concentration occasionally leads to a better kidney function being assumed than actually exists.

For patients with impaired kidney function or suffering from severe infections, especially patients suffering from a specific blood count abnormality (neutropenic patients) who would be receiving a daily ceftazidime dose of 6 g in the absence of kidney function impairment, the single dose stated in the table above can be increased by 50% or else the dosing interval can be shortened appropriately. Plasma ceftazidime levels must be monitored in these patients, minimum levels are limited at 40 mg/litre.

For children with impaired kidney function, creatinine clearance must be calculated on the basis of lean mass and the dosing interval increased as for adults.

Patients undergoing haemodialysis
The serum half-life of ceftazidime during haemodialysis ranges from 3 to 5 hours. After each haemodialysis phase, the corresponding maintenance dose of ceftazidime must be repeated.
The recommended daily dose for patients suffering from kidney failure and undergoing continuous arteriovenous haemodialysis or high-flux haemofiltration in the ICU is 1 g divided into several individual doses. The recommended dosage in conjunction with low-flux haemofiltration is the same as that for impaired kidney function.

Patients undergoing peritoneal dialysis (a specific procedure for cleansing the blood)
Ceftazidime is also suitable for patients undergoing peritoneal dialysis or continuous ambulatory peritoneal dialysis (CAPD), with the dose being adapted to the kidney function. For these patients, the initial ceftazidime dose may be 1 g, followed by 500 mg administered every 24 hours. In case of intraperitoneal infections, ceftazidime may moreover be administered together with the dialysis fluid (usually 125 to 250 mg per 2 litres of dialysis fluid).

Dosage in the presence of liver failure
A dose adjustment is not necessary, except in cases of concurrent kidney failure.

6.2 Notes on handling

Intramuscular administration:
Ceftazidime is prepared with water for injections Ph.Eur. or 0.5% or 1% lidocaine hydrochloride injection BP (British Pharmacopoeia), see details in the table below. The product information for lidocaine solutions must be read prior to preparation of ceftazidime with lidocaine.

Intravenous administration:
Water for injections Ph.Eur. is used for the preparation of ceftazidime for direct, intermittent intravenous administration (see table below). The solution is slowly injected directly into the vein over the course of 5 minutes or is administered via the tubing of an infusion set.
For intravenous infusions, the 500 mg or 1 g vial is admixed with water for injections Ph.Eur. or a compatible intravenous fluid and, using one of the compatible intravenous fluids, an adequate amount of the resultant solution is introduced into an intravenous container. Where compatible solutions are employed, an intravenous infusion can be carried out using an infusion set with a Y piece. However, it is desirable to interrupt administration of the other solution while a solution containing ceftazidime is being infused.

Preparation of ceftazidime solutions

diarrhoea occurs during treatment, ceftazidime must be discontinued and appropriate countermeasures instituted. Medicines which inhibit the movement of the intestines (antiperistaltics) are contraindicated. Ceftazidime must be used with caution in patients with known gastrointestinal disorders, in particular inflammation of the large intestine.
A harmful effect of ceftazidime on the kidneys has not been established. Nevertheless, the total daily dose must be reduced if ceftazidime is administered to patients with acute or chronic kidney failure, in order to prevent possible clinical consequences such as convulsions, for instance.
Cephalosporin antibiotics must be used with caution in patients being treated at the same time with medicines which may damage the kidneys, such as aminoglycoside antibiotics, or with strong diuretics (e.g. furosemide), since these combinations may impair kidney function and have been associated with irreversible damage to the brain nerves (see section on Interactions with other medicines).
As with other cephalosporins, long-term use of ceftazidime may lead to overgrowth of insensitive organisms such as Enterococci and Candida spp.
It is recommended that blood picture, and kidney and liver function are checked at regular intervals during long-term treatment with ceftazidime.
Ceftazidime has no effect on enzymatic determination of glucosuria. Minor interference with copper reduction methods (Benedict's test for glucose, Fehling's test, Clinitest) is possible.
Ceftazidime has no effect on the alkaline picrate assay for creatinine.
A positive outcome of the Coombs test in about 5% of patients in conjunction with the use of ceftazidime may affect serological cross-matching.
For patients requiring sodium restriction, the sodium content of the medicine must be taken into account (for 500 mg ceftazidime 26 mg sodium per dose and for 1 g ceftazidime 52 mg sodium per dose).

Pregnancy

Your doctor will decide on whether to use the medicine after careful risk/benefit assessment. Please inform your doctor when you find out that you are pregnant.

Breast-feeding

Ask your doctor or pharmacist for advice before taking any medicine.
Ceftazidime enters breast milk in small concentrations. The infant is therefore at a risk of developing diarrhoea, hypersensitivity or fungal growth on mucous membranes. Ceftazidime should be administered to breast-feeding women only if strictly indicated.

Driving and using machines:

⚠ Attention: This medicine may impair the speed of reactions and the ability to drive.
No studies of the effects on the ability to drive a vehicle and to use machines have been carried out. The possibility of dizziness or convulsions must be reckoned with when driving a vehicle or using machines.

Important information about some of the ingredients of Ceftazidim

Interactions with other medicines:

Please inform your doctor or pharmacist if you are taking or have recently taken any other medicines, even those not prescribed.
There have been reports of a kidney-damaging effect after simultaneous administration of cephalosporins and aminoglycoside antibiotics or strong diuretics such as furosemide. In view of the possible kidney-damaging and brain-damaging effect of aminoglycoside antibiotics, kidney function must be strictly monitored, especially if aminoglycosides are given in high dosages for long-term treatment.

An opposite effect of chloramphenicol on ceftazidime and other cephalosporins has been detected *in vitro*. Even though the clinical relevance of this knowledge is not known, the possibility of an opposite effect must

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

5. STORING PARZIDIM

Keep out of the reach of children!

Note the expiry date on the package.
Do not use this medicine after the expiry date stated on the package.
Do not store above 30° C. Store in the original package.
The prepared, ready-to-use solution must be used immediately.

From a microbiological point of view, it is recommended to use the solution immediately. If it is not used immediately, the user holds responsibility for duration and conditions of storage; the duration of storage does not usually exceed 24 hours at 2 to 8°C, provided the preparation of the solution was carried out under controlled and validated aseptic conditions.
You can dispose of expired and unused medicines in any pharmacy.

6. Notes on handling and use for doctors and healthcare professionals

6.1 Dosage

Method of administration

The product may be administered only by a doctor.

Parzidim 1 g – vial: Powder for preparing a solution for injection/infusion.
Ceftazidime can be administered intravenously or by deep intramuscular injection into a large muscle mass, for example into the upper outer quadrant of the large gluteal muscle or into the lateral thigh. For information on preparation of the solutions for intravenous or intramuscular administration see Notes on handling (6.2).

Dosage

The usual dosages for the various age groups defined for patients with normal kidney function are:

Age group	Infection	Usual dose
Adults	Most frequent uses	1 g every 8 hours **OR** 2 g every 12 hours
	Severe infections and infections in patients with blood count abnormality	2 g every 8 hours **OR** 3 g every 12 hours
	Urinary tract infections	500 mg every 12 hours **OR** 1 g every 12 hours
	Prophylaxis in surgical removal of the prostate gland	1 g for induction ± 1 g upon removal of catheter
	Cystic fibrosis	100-150 mg/kg/day divided into three doses; no more than 9 g/day
Elderly patients	Any infections, in particular in patients older than 80 years	No more than a total of 3 g a day[1]
Infants > 2 months, toddlers and children	Most frequent uses	30-100 mg/kg/day divided into two or three doses
	Severe infections	Up to 150 mg/kg/day (max. total of 6 g per day) divided into 3 doses
Full-term newborn babies and infants below the age of 2 months	Most frequent uses	25-60 mg/kg/day divided into two doses[2]

[1] *In acutely ill elderly patients, ceftazidime clearance is often decreased.*
[2] *The plasma elimination half-life of ceftazidime may be 3 to 4 times longer than in adults.*

	Amount of the diluent to be used (ml)	Approximate volume available (ml)	Approximate Ceftazidime concentration (mg/ml)
Intramuscular			
500 mg	1.5	2.10	238
1 g	3.0	3.80	263
Intravenous			
500 mg	5	5.50	91
1 g	10	11.00	91

*** Note: Addition must take place in 2 steps (see 'Instructions for preparation' below)**

Carbon dioxide is released during dissolution of ceftazidime; this produces a positive pressure. Compliance with the recommendations for preparation given below will enable problem-free use.

Instructions for preparation:
For 500 mg i.m./i.v. and 1 g i.m./i.v. vials
1. Inject diluent and shake thoroughly to dissolve. The vacuum in the vials makes injection of the diluent easier.
2. Carbon dioxide is released during dissolution of the antibiotic, which produces pressure within the vial. The solution turns clear within 1 to 2 minutes.
3. Turn the vial upside down and push the syringe plunger all the way in before insertion.
4. Introduce the needle through the rubber stopper of the vial. Always keep the needle tip immersed in the solution and withdraw the vial contents as usual. The pressure within the vial renders withdrawal easier.
5. The withdrawn solution may contain carbon dioxide bubbles which must be removed from the syringe prior to injection.

Note: To retain sterility of the product, please ensure not to pierce the aeration needle through the vial stopper until the product has dissolved completely.
For single use only.
Unused solution must be discarded.
Only clear solutions with virtually no particles may be used.
Free of bacterial endotoxins.
The colour of ceftazidime solutions ranges from pale yellow to amber and depends on the concentration, the diluent and the storage conditions. On compliance with the recommendations given, the efficacy of the medicine is not impaired by these colour variations.
For ceftazidime concentrations between 20 mg/ml and 333 mg/ml, Parzidim powder for preparing a solution for injection/infusion can be dissolved in commonly used infusion solutions:
0.9 % sodium chloride solution (physiological saline solution),
5 % glucose solution,
0.9 % sodium chloride + 5% glucose solution,
Ringer's lactate solution
For intramuscular administration, Parzidim powder for preparing a solution for injection/infusion may also be diluted with 1% strength lidocaine solutions.

Incompatibilities

Ceftazidime must not be mixed with solutions having a pH above 7.5, such as sodium bicarbonate solution, as additive to injections. Owing to the risk of precipitation, ceftazidime and aminoglycosides must not be mixed in the injection solution.
To prevent precipitation, cannulae and catheters for intravenous use must be rinsed with physiological saline solution between administrations of ceftazidime and vancomycin.

Date of the information: July 2005

If you need further information regarding Parzidim vials, please contact your doctor or pharmacist.